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SELF-ADMINISTRATION OF 4-METHYLMETHCATHINONE (MEPHEDRONE; 'MEOW MEOW') IN WISTAR AND SPRAGUE-DAWLEY RATS.

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Aims: Very little is known regarding the abuse liability or the behavioral and physiological effects of 4-methylmethcathinone (4-MMC; aka Mephedrone or 'meow meow'). However, increased recreational use of 4-MMC has generated a great need for such knowledge.
Methods: In this study we present data from intravenous self-administration experiments using two different rat strains (Wistar and Sprague-Dawley). Some of the groups were implanted with radio transmitters for reporting activity and body temperature.
Results: Intravenous self-administration of 4-MMC was established in both strains on an FR5 schedule and resulted in stable intake patterns within 10 sessions. After initial acquisition, dose-dependent rates of responding were observed across a tested range of 0.05-2.0 mg/kg/infusion. Additionally, similar dose-response relationships for 4-MMC self-administration were observed in a group of Sprague-Dawley rats previously trained to self-administer methamphetamine. In Wistar rats, activity counts were increased by self-administration of 4-MMC. In Sprague-Dawley rats, body temperature was decreased in a dose-dependent manner by self-administration of 4-MMC (an effect that may be more similar to that caused by bolus administration of MDMA). Lastly, Sprague-Dawley rats were more sensitive to the thermoregulatory effects of 4-MMC while Wistar rats were more sensitive to the locomotor-stimulant effects.
Conclusions: Additional study is required to resolve the observation that behavioral effects differed between the two strains of rats. Nonetheless, these initial data indicate that 4-MMC has an abuse liability that is similar to that of amphetamine-class drugs of abuse. Moreover, the observed decrease in body temperature may be related to user reports of cooling and tingling sensations in the extremities.
Financial Support: This work was supported by USPHS grants DA018418 and DA024705

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DRUG USE HISTORY AMONG PATIENTS IN SUBSTITUTION THERAPY IN BUCHAREST, ROMANIA.

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Aims: In order to improve the services offered in our first and still single harm reduction approach MMT center we have analyzed the drug use history among our patients. Due to the economic crisis we are offering now almost only paid services. We have 158 men and 68 women. 65% of our patients are gypsies.
Methods: Our study was a prospective one, analyzing 29 items through an anonymous questionnaire based on items from YRBSS. We have asked about age at first use for different drugs both legal and illegal, about life and last month use.
Results: We have obtained complete questionnaires from 148 patients 68 women and 80 men. 64 of them were gypsies. Among the rroma population the alcohol consumption was earlier both in men and women compared to Caucasians. Marijuana use was more frequent in Caucasians. LSD, cocaine and Extazy have comparable use. Inhalants are practically not used. Benzos and barbiturates are more used by women than men. The new "legal" drugs (especially mephedrone and methamphetamines) are more used by caucasians than gypsie's.
Conclusions: The data show the need for interventions among school childrens in order to reduce alcohol use and binge drinking and especially to prevent the increase in the new "legal" drugs who have already produced more than 18 death in only one year from their arrival on the market.
Financial Support: This work did not receive any financial support.

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THE MARIJUANA-MOOD ASSOCIATION DURING EARLY-MID ADOLESCENCE.

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Aims: Associations linking marijuana smoking with negative mood states have been reported. Here, the aim is to estimate the degree to which mood states measured in early adolescence might predict occurrence of marijuana smoking by mid-adolescence in an urban African American cohort, with a hypothesis that the association might be stronger for females.
Methods: This study was conducted in the context of the Miami Prenatal Cocaine Study (MPCS), a longitudinal study of 476 full-term African American prenatally cocaine-exposed (PCE; n=253) and non-cocaine-exposed (NCE; n=223) infants enrolled at birth and followed serially through age 16/17 years. A total of 407 (86%) were seen at least one of the 12-, 14/15-, and 16/17-year study visits, when marijuana exposure was assessed by confidential self-report as well as hair and urine assays. Symptoms of depression and anxiety were assessed via the self-report Child Depression Inventory and the Revised Children's Manifest Anxiety Scale, respectively, at the 12-year visit. Odds ratio estimates of the predictive association (OR) are from the generalized linear model with generalized estimating equations.
Results: The estimated occurrence of marijuana smoking by mid-adolescence was not predicted by the age 12 depression level ($p>0.3$) or anxiety level ($p>0.1$). Being male did predict onset of marijuana smoking between age 12 and age 16/17 ($p<0.05$), but there was no evidence to support that the marijuana-mood association might be stronger for females than for males (product-term $p>0.05$), except in cross-section at age 12 ($p<0.05$).
Conclusions: Negative mood did not predict occurrence of marijuana smoking across the years from early to mid adolescence. The association between marijuana and negative mood may be stronger for females than males in early adolescence. Otherwise, contrary to expectation, there was no male-female variation in marijuana-mood association.
Financial Support: NIH ORWH and NIDA: P50DA024584, R01DA006556; K01DA016720.

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INHIBITING GLYCINE TRANSPORTER-1 DURING EXTINCTION TRAINING ATTENUATES REACQUISITION OF COCAINE SELF-ADMINISTRATION IN SQUIRREL MONKEYS AND RATS.

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Aims: Extinction training has been implemented as a means to reduce the salience of cocaine-associated cues and prevent relapse. Because of cognitive deficits associated with protracted cocaine use, cognitive enhancers that act by increasing glycine transmission at the NMDA receptor might be useful in promoting extinction learning. The present study investigated the ability of a selective glycine transporter-1 inhibitor, Org 24598, to facilitate extinction learning and attenuate the reacquisition of cocaine self-administration.
Methods: Subjects were trained to self-administer cocaine under a second-order FI(FR) schedule in which responding was controlled by i.v. cocaine injections and a cocaine-paired visual stimulus. During three successive weekly 1-hr extinction sessions in which completion of each FR unit produced the cocaine-paired stimulus, but no cocaine injections, squirrel monkeys (n=6) were pretreated with Org 24598 (1.0 mg/kg; i.m.) or vehicle and rats were pretreated with Org 24598 (3.0 mg/kg; i.p.; n=5) or vehicle (n=3). One week following the last extinction training session, cocaine injections were restored and reacquisition of cocaine self-administration was evaluated daily for 15 sessions.
Results: Compared to vehicle, Org 24598 administered during extinction training significantly deterred reacquisition of cocaine self-administration up to the 5th reacquisition session in both monkeys and rats. In control tests, Org 24598 administered prior to weekly cocaine self-administration sessions did not significantly alter responding relative to baseline.
Conclusions: These results support the application of compounds that act via glycine transporter inhibition to promote extinction learning and subsequently reduce relapse to cocaine self-administration.
Financial Support: NIH/NIDA grants DA024315 & RR00168

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THE EFFECTS OF NICOTINE AND NON-NICOTINE COMPONENTS OF CIGARETTE SMOKING ON CEREBRAL BLOOD FLOW.

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Aims: Smoking behavior involves exposure to nicotine, as well as distinct sensorimotor factors. Putatively, these factors play a role in tobacco smoking and addiction. Whereas the effects of smoking versus abstinence on cerebral blood flow (CBF) have been examined, little is known regarding the unique contribution of nicotine and non-nicotine components to these effects. This was investigated in a preliminary study in which nicotine patches and denicotinized cigarettes were administered in a factorial design.
Methods: 20 smokers underwent a 7 min resting state perfusion MRI scan (pASL FAIR) on 4 occasions, following 24 hours in each condition: 1) 21mg nicotine patch + denicotinized (denic) cigarette smoking, 2) placebo patch + denic smoking, 3) nicotine patch + no smoking, and 4) placebo patch + no smoking. Condition orders were counterbalanced. Significant effects were identified at a cluster corrected threshold of $p < .005$, $k=33$. CBF was preprocessed and analyzed using SPM8.
Results: A global analysis of whole brain gray matter CBF found no effects of nicotine or cigarette smoking. Regional analyses found a main effect of cigarette (denic > no smoking) in the left temporal lobe, including the superior temporal gyrus, limbic lobe and hippocampus, and fusiform gyrus. There was also an interaction effect in the inferior, middle, and superior frontal gyri (nicotine+denic > placebo+no smoking > nicotine+no smoking = placebo+denic). Main effects of nicotine were not observed.
Conclusions: These preliminary data suggest that neither nicotine nor other components of cigarette smoking (i.e., carbon monoxide) affect global cerebral blood flow among regular daily smokers. Regionally, smoking denic cigarettes appears to enhance blood flow to areas subserving associative learning and memory; the effects of smoking on cognitive control regions appear to be moderated by the presence of nicotine.
Financial Support: This work was supported by National Institute of Drug Abuse grant R01DA023516.

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ALCOHOL DEPENDENCE CLINICAL FEATURES AND EXPERIENCES OBSERVED SOON AFTER ONSET OF DRINKING: MALE-FEMALE VARIATIONS.

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Aims: During the first weeks and months after onset of drinking, some newly incident drinkers start to have experiences that resemble clinical features associated with alcohol dependence (CF). In this research report, we seek to estimate the occurrence of these experiences as well as associations with being male or female.
Methods: Data are from the United States National Surveys of Drug Use and Health, 2004-2007, with nationally representative samples of non-institutionalized civilian residents that yield 4,876 newly incident drinkers (all with drinking onset within 180 days before assessment). Standardized assessments are made for newly incident drinking, CF experienced since drinking onset, and the covariates under study. Statistical analysis involves standard methods for estimation of cumulative incidence proportions and relationships of interest.
Results: Within 180 days after drinking initiation, an estimated 1 in 6-7 newly incident drinkers have started to set limits on drinking, with little male-female (M-F) variation; 1 in 7 have tried to stop or cut down on drinking, also with modest M-F variation. As might have been expected, occurrence of general medical or physical problems due to drinking emerged quite rarely within 180 days after drinking onset, with no noteworthy male-female variation in the data under study here.
Conclusions: Within 180 days after the onset of drinking, a substantial number of drinkers are having experiences that resemble the clinical features of alcohol dependence. Whereas there is robust evidence of male-female differences in occurrence of alcohol dependence syndromes, the current evidence suggests male-female parity in occurrence of the early proto-CF drinking experiences arising soon after onset of drinking. This work sets the stage for new research on these very early stages of alcohol involvement and problem-related drinking experiences.
Financial Support: NIDA support: T32DA021129 (OAA); K05DA15799 (JCA)].

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THE MISSOURI SCREENING, BRIEF INTERVENTION AND REFERRAL TO TREATMENT PROGRAM: SIX-MONTH OUTCOMES.

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Aims: A growing body of research and clinical data indicates that screening and brief intervention reduces consumption of alcohol and drugs, increases levels of abstinence, and significantly reduces ongoing medical costs associated with substance use. The Missouri Screening, Brief Intervention, Referral and Treatment (MOSBIRT) initiative has been implemented with a grant from SAMHSA. Implemented in different medical settings at multiple sites throughout the State, the initiative screens for and identifies individuals at risk for substance related problems. Those screening at-risk are provided brief interventions focusing on increased awareness regarding substance use, and motivation toward behavioral changes. The purpose of this study is to determine to what extent the MOSBIRT affects patients' pattern of use at a 6 month follow-up at various medical settings as a part of routine care.
Methods: A random sample of patients receiving an intervention is administered the Government Performance and Results Act measure at baseline and again at 6 months. These patients were asked the number of days they used alcohol and illegal substances in the last 30 days.
Results: Initial findings from the first set of follow-up interviews (N=37) indicate that average days of use of all substances had declined substantially six months following MOSBIRT services at the following rates: alcohol—21%, binge drinking (5+ drinks)—44%, alcohol and drug—43%, illegal Drug—59%, marijuana—28% . Due to a small sample size, the results are considered preliminary, but the results point to large effect size reductions in the use of substances.
Conclusions: MOSBIRT's initial findings are similar to the outcomes of previous SBIRT literature, indicating that those patients receiving a brief 10-15 minute intervention in a medical setting had substantial reductions in substance use at follow-up. The brief intervention is administered by trained health coaches using Motivational Interviewing techniques.
Financial Support: TI 019549

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EFFECTS OF ALCOHOL ON SEROTONIN (5-HT3) RECEPTOR: THE ROLE OF HISTONE DEACETYLASES AND THEIR INHIBITOR TRICHOSTATIN A.

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Aims: Previous Studies have demonstrated that alcohol abuse is a complex addiction regulated by multiple mechanisms such as neurotransmitter 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 class I HDACs such as HDAC1, 2, 3 and 8.
Methods: To test the effects of alcohol on 5-HT3 and HDACs, the human neuronal cell line, SK-N-MC was treated with different concentrations of EtOH, and the gene and protein expression of 5-HT3 and HDACS 1, 2, 3, and 8 were assessed at different time points. Furthermore, cells were also treated with the histone deacetylase inhibitor, Trichostatin A (TSA), and the effects on gene expression were evaluated by quantitative PCR and protein expression by western blot and flow cytometry. HDAC activity was also measured by a fluorescent assay.
Results: Our results show alcohol treatment modulates 5-HT3 and HDACs. Furthermore, there is a dose dependent increase in HDAC enzymatic activity after alcohol treatment. Pharmacological inhibition of HDACs with Trichostatin A (TSA) significantly enhanced the ethanol effects on 5-HT3 expression, and this effect can be blocked by the 5-HT3 antagonist, Ondansetron.
Conclusions: Since alcohol regulates serotonin receptors and histone deacetylases play an important role in the modulation of 5-HT3, the use of HDAC inhibitors may be of therapeutic significance in alcohol-related disorders.
Financial Support: This work was supported in part by the National Institute on Drug Abuse grants R37DA025576 and R01DA021537.

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A NOVEL BUPRENORPHINE MAINTENANCE TREATMENT PROGRAM IN A COMMUNITY-BASED RECOVERY CENTER IN BALTIMORE CITY: INITIAL TREATMENT OUTCOMES.

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Aims: To provide an overview of a community-based application of buprenorphine induction and maintenance treatment, describe the sociodemographic and clinical characteristics of clients served, and present initial findings relevant to increasing access to treatment and reducing illicit opioid use.
Methods: The study sample includes all Baltimore city clients served by the program from inception in July 2010. Client sociodemographics, substance use, behavioral and primary health care treatment histories, and health status were abstracted from a retrospective review of client records. Data on the weekly use of buprenorphine, heroin, and other substances were collected via client and urine toxicology reports. Information on client transition to traditional clinics for ongoing maintenance treatment was also collected. The data analysis (presently ongoing) will summarize characteristics of clients served and the program's effectiveness in reducing opioid and other illicit substance use.
Results: As of December 2010, the program has served 38 clients. Preliminary findings indicate that clients who engage in treatment for greater than one month are likely to maintain positive buprenorphine and negative opiate urine toxicology screens for the remainder of treatment.
Conclusions: Buprenorphine maintenance treatment has been demonstrated effective for opioid dependence in clinical settings. Preliminary findings from this study suggest that buprenorphine treatment for opioid dependence can be effectively incorporated into community-based recovery centers, and that clients' use of opiates decrease over time. The adoption of similar programs in other non-traditional community sites may increase access to appropriate treatment for individuals otherwise unable or unwilling to receive it.
Financial Support: The evaluation and research study are supported by the Behavioral Health Leadership Institute and the Open Society Institute.

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MALE-FEMALE VARIATION IN EARLY RECEIPT OF ALCOHOL TREATMENT SERVICES SOON AFTER DRINKING ONSET.

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Aims: This study's aim is to study male-female variations in alcohol treatment entry soon after onset of drinking, as observed in a nationally representative sample of newly incident drinkers.
Methods: Data are from the United States 2004-2008 National Surveys on Drug Use and Health (NSDUH), which yields a nationally representative sample of 20,481 newly incident drinkers, all with drinking onset within a 24 month time interval prior to standardized assessment. NSDUH also assesses receipt of alcohol treatment services in primary care and specialty settings. The analysis approach includes estimation of cumulative incidence proportions and regression modeling, with p-values and 95% confidence intervals for complex sample survey data.
Results: An estimated 1.1% of ever-drinkers had recently received alcohol treatment services, with robust male-female variation; males, 1.6%; females, 0.6%. This male-female variation was not observed for the newly incident drinkers ($p>0.05$), even though the male newly incident drinkers have higher drinking rates than females.
Conclusions: It appears that male-female differences in receipt of alcohol treatment services do not emerge soon after drinking onset. Greater understanding of variations in use of these services could lead toward more effective early screening, brief intervention, and referral to treatment approaches, as well as improved patient outcomes.
Financial Support: NIDA award K05DA015799 JCA.

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MENSTRUAL PHASE DIFFERENCES IN SUBJECTIVE-EFFECTS OF NICOTINE RESPONSE.

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Aims: Compared to men, women are more likely to relapse to smoking after a quit attempt. While the specific causal mechanisms for this sex difference remain unknown, recent research indicates sex hormones may play a role. Therefore, we aimed to test the hypothesis that subjective-effects (SE) of nicotine response will vary by menstrual phase.
Methods: Female subjects (n=66) were between the ages of 18-40, with regular menstrual cycles who smoked ≥5 cigarettes/day. Subjects were randomly assigned to attend a two-hour nicotine response session during either the Follicular (F) or Luteal (L) phase. Subjects refrained from smoking at least 30 minutes prior to the start of the session. At Time 0 subjects used nicotine nasal spray as a nicotine challenge. At Time -30, 5, 20, 30 and 60 minutes subjects rated their levels of the following eight SE using a 100-point Visual Analog Scale: Stimulation, Head Rush, Jittery, Relaxed, Pleasant, Dizzy, Alert, and Urge to Smoke. To assess differences by menstrual phase, simple t-tests were used to compare absolute levels of SE and repeated measures regression analyses were used to investigate the change in SE during the session.
Results: Subjects were 29.8±6.5 years of age and smoked 13.3±6.2 cigarettes per day. There were no significant differences in demographics or smoking behavior by testing phase (F: n=33; L: n=33). Three significant differences in absolute levels of SE were observed including Pleasant at Time -30 (F: 73.3±21.9; L: 62.1±20.5; p=0.05), Alert at Time 5 (F: 63.2±20.4; L: 74.3±19.9; p=0.03) and Pleasant at Time 30 (F: 61.6±24.8; L: 73.0±20.7; p=0.04). Menstrual phase significantly improved the fit of all eight regression models and was a significant, independent predictor for change of three SE: Stimulated (t=2.20, p=0.03), Pleasant (t=2.25, p=0.03), and Alert (t=2.31, p=0.02).
Conclusions: The results of this study indicate that there may be menstrual phase differences in subjective-effects of nicotine response. If confirmed by a larger study, these results suggest that vulnerability for relapse after a lapse may vary by menstrual phase.
Financial Support: NIDA 5R01-DA08075

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A DISABILITY-ADJUSTED CANNABIS WITHDRAWAL SCALE REVEALS WITHDRAWAL SYMPTOMS ASSOCIATED WITH RELAPSE.

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Aims: The primary aim is to develop and test the psychometric validity of a cannabis withdrawal scale that considers the clinical significance of symptoms. The secondary aim is to explore the link between withdrawal and cannabis relapse.
Methods: A withdrawal scale was developed that included a measure of symptom disability. The scale was tested on 45 DSM-IV dependent cannabis users in their home environment during a one week control phase and a two week cannabis abstinence phase.
Results: The most prominent disability adjusted cannabis withdrawal symptoms were sleep disturbance (e.g. insomnia Wald χ^2=57, p = 0.003), mood disorder (e.g. mood swings; Wald χ^2=49, p = 0.03), restlessness (Wald χ^2=31, p = 0.03), cravings (Wald χ^2=32, p = 0.005) and physical tension (Wald χ^2=35, p = 0.014). Within the ten people who relapsed, physical tension (Wald χ^2 = 4.43, p = 0.035), cravings (Wald χ^2= 5.04, p = 0.025) and mood swings (Wald χ^2 = 4.32, p = 0.038) were all significantly elevated above baseline measures on the day of relapse. Physical tension alone was significantly higher in people who relapse than in those who don't ($F_{1,44}$ = 4.9, p = 0.03). People who relapsed reported being significantly more tolerant of distress at baseline than did people who did not relapse ($F_{1,44}$ = 5.6, p = 0.03).
Conclusions: Adjusting cannabis withdrawal symptoms by disability enables a novel view of the relative clinical significance of symptoms. The relationship between cannabis withdrawal and relapse suggests that cannabis withdrawal is clinically significant. The distress tolerance finding suggests that users who relapse have lower levels of insight, which may lead to poor planning for quit attempts. Treatment developments should explore the impact of mindfulness and insight development.
Financial Support: Commonwealth Department of Health and Ageing, Australia

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CHRONIC MORPHINE TREATMENT INFLUENCES MU-OPIOID RECEPTOR AGONIST EFFECTS ON INTRACRANIAL SELF-STIMULATION.

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Aims: Intracranial Self-Stimulation (ICSS) is one behavioral assay used to evaluate abuse-related effects of mu opioid agonists and other drugs. Facilitation of ICSS is often interpreted as an abuse-related drug effect. Many factors can influence mu agonist effects on ICSS, including drug efficacy at mu receptors, dose and pretreatment time. This study tested the hypothesis that mu opioid agonist effects on ICSS are determined in part by the degree of opioid dependence and tolerance.
Methods: Adult male Sprague-Dawley rats were equipped with electrodes targeting the medial forebrain bundle. Stimulus intensities were individually determined for each rat, and during daily behavioral sessions, 10 stimulus frequencies (56-158 Hz) were available under an FR1 schedule. The primary dependent measure was rate of reinforcement at each frequency. Once ICSS stabilized, fentanyl (0.001-0.1 mg/kg SC, 30 min pretreatment) was tested under conditions of chronic treatment with saline, low-dose morphine (3.2 mg/kg/day) or high-dose morphine (18 mg/kg/day). Behavioral sessions were conducted 23 hr after each daily morphine injection, at a time after dissipation of any direct morphine effects.
Results: Consistent with previous findings, chronic morphine treatment produced a dose-dependent rightward shift in baseline ICSS frequency-rate curves determined 23 hr after daily morphine administration and immediately before fentanyl administration. During chronic saline treatment, fentanyl produced only a dose-dependent decrease in ICSS. Chronic morphine produced a dose-dependent tolerance to fentanyl-induced rate-decreasing effects and an increase in expression of fentanyl-induced facilitation of ICSS.
Conclusions: Chronic morphine produced (1) dependence as indicated by withdrawal-associated decreases in baseline ICSS 23 hr after daily morphine treatments, (2) tolerance to mu agonist-induced rate-decreasing effects and (3) an increase in expression of abuse-related facilitation of ICSS produced by mu agonists.
Financial Support: Supported by NIH grant R01 NS070715

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COCAINE SELF-ADMINISTRATION MODIFIES HIPPOCAMPAL NEURON MORPHOLOGY IN LEWIS RATS.

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Aims: Chronic exposure to drugs of abuse is thought to induce a variety of persistent changes in both behavior and brain morphology, including modifications of neurons from the brain regions involved in addiction. There are evidences that support a role for the hippocampus in cocaine addiction. Previously, we have showed that cocaine appears to facilitate the induction and maintenance of different forms of hippocampal long-term potentation, and that there were differences in hippocampal synaptic plasticity between Lewis (LEW) and Fischer 344 (F344) rats after chronic cocaine administration. The aim of the present work was to test if cocaine self-administration (1 mg/kg) or saline (0,9% NaCl) could affect to the morphology of the CA1 hippocampal neurons in LEW and F344 rats.
Methods: After three weeks of self-administration behavior, both inbred rat strains clearly self-administered more cocaine than saline, but there were not significant differences in the number of cocaine injections between them. Immediately after the last self-administration session, the animals were intracardially perfused with 4% paraformaldehyde, their hippocampal neurons intracellularly injected with Lucifer Yellow in fixed tissue, and reconstructed in three dimensions using Neurolucida software.
Results: Compared to saline, cocaine self-administration produced a statistical significant increment in the spine density of hippocampal neurons in LEW rats with no effects in F344 rats
Conclusions: These results suggest a differential cocaine effect on hippocampal neuron morphology depending upon the genetic background of individuals.
Financial Support: Supported by grants from: Ministerio de Ciencia e Innovación (SAF2007-064890); Ministerio de Sanidad y Consumo (Instituto de Salud Carlos III: RD06/001/0029 and Plan Nacional sobre Drogas 2008-2010);Comunidad de Madrid (S-SAL/0261/2006;Consorcio CANNAB-CM);and UNED (Plan de Promoción de la Investigación).

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PREDICTORS OF DISCUSSING HIV TESTING WITH CUSTOMERS AMONG PHARMACY STAFF REGISTERED IN THE NEW YORK STATE EXPANDED SYRINGE ACCESS PROGRAM: PRELIMINARY FINDINGS FROM THE PHARM-HIV STUDY.

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Aims: HIV is high among black and Hispanic injection drug users (IDUs). The New York State Expanded Syringe Access Program (ESAP) allows registered pharmacies to sell sterile syringes to IDUs to prevent HIV. Pilot data shows that providing prevention services in ESAP pharmacies is feasible. We used baseline data from our Pharmacists as Resources Making Links to HIV Testing (PHARM-HIV) study to examine individual and pharmacy level factors associated with discussing HIV testing with customers among ESAP-registered pharmacy staff in Harlem.
Methods: 18 ESAP-registered pharmacies were selected in Harlem, NY. A 10-minute survey was administered to syringe selling pharmacy staff. Bivariate analysis was conducted using t-tests, chi-square tests or Fisher's exact test
Results: Of 79 pharmacy staff, 68.4% were non-pharmacists and female. Overall, 30.4% had discussed HIV testing with their customers, 91.4% supported providing HIV testing referrals, and 70.9% supported in-pharmacy HIV testing. Those that had ever discussed HIV testing with customers were more likely male (p=0.0205), pharmacists (p=0.0045), work more years in pharmacies (p=0.0326), supportive of ESAP (p=0.0083), and provide daily in-pharmacy counseling on prescription medications (p=0.0016), medical conditions (p=0.0051), and other products (p=0.0318)
Conclusions: There is support for in-pharmacy HIV testing services among pharmacy staff in ESAP-registered pharmacies in neighborhoods with high drug activity, and HIV testing can be comfortably discussed. The expansion of HIV testing referrals and in-pharmacy testing, and the training of pharmacy staff on how to engage in HIV testing and risk reduction counseling with their syringe customers should be explored.
Financial Support: CDC

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INDIVIDUAL DIFFERENCES IN RESPONSE TO NOVELTY ASSOCIATES WITH BINGE-LIKE PALATABLE FOOD INTAKE.

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Aims: Patterns of individual differences in novelty-responsivity and -seeking can be seen with respect to the development and maintenance of drug dependence, eating disorders, and obesity. The goal of the present study was to establish a link between high novelty-responsivity and/or -seeking with binge eating behavior using rodent animal models.
Methods: Naïve male rats were initially placed in low-light inescapable open field monitors for 30 min and total ambulation recorded to differentially identify novelty-responsivity. The upper and lower 25% of rats were identified as high responders (HR) and low responders (LR), respectively. One week later, the upper and lower 50% of HR/LR rats were identified as high novelty preference (HNP) and low novelty preference (LNP) in a free-choice procedure, respectively. Standard brown rodent chow (LabDiets 5001; 3.7% sucrose/4.5% fat by weight) was replaced with palatable rodent chow (35% sucrose/4.3% fat by weight) ad libitum for 6 days. After this acclimation, period rats were returned to standard brown chow diet for 5 days ad libitum and were then allowed unrestricted access to the palatable chow for 2 hrs to investigate binge-eating behavior.
Results: HR rats displayed significantly higher total ambulation vs. LR rats. HNP rats spent a higher amount of time in the novel environment vs. LNP rats. Individual rats displayed a mix of novelty-response vs. -seeking phenotypes, i.e. not all HR rats expressed the HNP phenotype. LR rats exhibited significantly higher levels of binging behavior on palatable vs. standard rat chow compared to HR rats ($p<0.05$).
Conclusions: Individual differences in the novelty-responsivity trait underlie binge-intake of a palatable food and sensitivity to uncontrolled intake of palatable food may be encoded by the individual's genotype together with the influence of environmental variables.
Financial Support: Jeane B. Kempner Scholarship, DA06511, DA024157, DA020087

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LONG-TERM BLOCKADE OF COCAINE SEEKING IN RATS TREATED WITH A COCAINE HYDROLASE VIRAL VECTOR.

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Aims: Cocaine dependence is a pervasive disorder with high rates of relapse. In a previous study, direct administration of a quadruple mutant albumin-fused butyrylcholinesterase (BChE) acutely blocked cocaine seeking in an animal model of relapse and abolished cocaine-induced seizures and lethality. In the present experiment we extended these results to a gene transfer paradigm using a related BChE mutant termed "CocH". Our aim was to determine if a single iv delivery of adenovirus vector encoding this enzyme (CocH vector) would block the reinstatement of cocaine seeking for an extended period of time.
Methods: Male and female rats were trained to self-administer 0.4 mg/kg cocaine under a fixed-ratio 1 (FR 1) schedule of reinforcement and were allowed to maintain this behavior for approximately 14 days. Following the final self-administration session, rats were injected with saline or the CocH vector, and their cocaine solutions were then replaced with saline. Rats were then allowed to extinguish lever pressing for 14 days. Subsequently, they were tested for drug-primed reinstatement during an 8-day reinstatement procedure by administering ip priming injections of saline (S), cocaine (5, 10, and 15 mg/kg, C), and d-amphetamine (A) according to the following sequence: S, C, S, C, S, C, S, A. Cocaine priming injections were then given once weekly for 4 weeks and then once monthly for up to 6 months following CocH vector or vehicle treatment.
Results: Administration with CocH vector produced substantial and sustained cocaine hydrolase activity in plasma and diminished cocaine- (but not amphetamine-) induced reinstatement responding for up to 6 months following treatment (compared to saline-treated controls).
Conclusions: These results demonstrate that viral transfer of CocH may be useful in preventing relapse to cocaine addiction for an extended period of time.
Financial Support: Supported by NIDA grants: DP1 DA031340, R01 DA023979 (SB; MEC subcontractor) and K05 DA015267 (MEC)

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GENDER AND RACE DIFFERENCES IN PRE-ADMISSION EKG FINDINGS AT A METHADONE CLINIC.

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Aims: While rates of EKG abnormalities in the general population are relatively low (e.g. QTc prolongation 0.05%, early repolarization variants [ERV] 6%, left ventricular hypertrophy [LVH] 6%), there have been concerns that methadone maintenance treatment may be associated with cardiac abnormalities. The aim of this study was to determine the rate of pre-treatment EKG abnormalities in persons presenting for methadone treatment, and to see if these varied as a function of gender, race, and recent cocaine use.
Methods: Demographic information, initial toxicology screen and EKG data (QTc interval, ERV, LVH) were analyzed for 242 subjects prior to admission to a methadone clinic. EKGs were reviewed by a physician. Differences between demographic groups were compared using chi-squared analysis.
Results: Average age was 41 years, years of education 11. 45% were female. 42% were African American, 57% Caucasian, and 1% Hispanic. The overall proportion of patients with QTc prolongation was 6%, ERV 25% and LVH 19%. 1 subject required immediate emergency room referral before admission due to an EKG abnormality. Women had lower rates of QTc prolongation vs. men (2% vs. 9%) and ERV (12% vs. 36%) (both $p<0.05$). ERV was higher in Caucasians compared to African Americans (31% vs. 16%) as was LVH (26% vs. 9%) (both $p<.05$). Subjects with cocaine negative urine toxicology at intake had a higher rate of QTc prolongation (15%) than those with a positive test (5%), $p<0.05$.
Conclusions: The lower rate of QTc/ERV in women and ERV/LVH in African Americans suggest potential moderators that merit further characterization. Gender and racial differences prior to methadone induction point to the need to control for such differences when examining in-treatment EKG findings. Examination of past cocaine use and concomitant medications is also needed to understand their potential influence on current EKG findings. Though EKG abnormalities rarely affected admission to the clinic, these analyses demonstrate high rates of EKG abnormalities in persons presenting for methadone treatment.
Financial Support: NIDA RO1DA021808, NIDA K24DA023186

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HCV-THERAPY IN OPIOID-DEPENDENT, SUBSTITUTED PATIENTS IN GERMANY.

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Aims: Studies indicate good chances of successful hcv-treatment in opioid dependent, substituted patients. Concerning patient's compliance studies revealed advantages of the closely monitored substitution treatment setting for achieving high retention. Nevertheless many physicians still hesitate to offer hcv-positive opioid dependent patients in substitution therapy an antiviral treatment. This work will describe which factors influence the compliance of opioid dependent, substituted patients in routine care.
Methods: Data is based on the national multicentre observational study SUPPORT in N=246 patients of N=36 physicians. N=242 data sets were included in the final analysis. The sample is divided in n=133 completer and n=109 dropouts. These two groups were analyzed concerning differences in psychiatric and somatic comorbidity, selected laboratory parameters and sociodemographic variables.
Results: More women complete their antiviral treatment for hcv than men. On average completers are 1 year younger than dropouts. Significantly more completer had no diagnosed psychiatric comorbidity before start of hcv-treatment. Completer started with a slightly higher dose of peginterferon than dropouts. More dropouts had an antiHBs-value >100, were positive for antiHAV, had hcv-genotype 1 or 4, a significantly higher HADS anxiety score and a higher HADS depression score.
Conclusions: The results reveal that specific parameters such as sex, hcv-genotype and psychiatric comorbidity may influence the compliance of opioid dependent, substituted patients in hcv-treatment. Physicians should monitor patients with disadvantageous preconditions during antiviral hcv-treatment more closely. A stable substitution treatment and the associated setting alone are not sufficient for high compliance during hcv-treatment. The psychiatric and somatic comorbidity should be analyzed in detail before start of the antiviral treatment and included in the therapy plan.
Financial Support: Study conducted by Essex Pharma GmbH. No financial support for preparation of abstract/poster.

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DIVERSION AND ABUSE OF BUPRENORPHINE: PATIENT SURVEY.

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Aims: Diversion and abuse of substance abuse medications is a threat to their continued approval and development. Buprenorphine approved for treating opioid-dependent patients has abuse potential. Because they may be aware of new illegal drugs on the street, applicants for substance abuse treatment may offer a perspective on diversion and abuse of buprenorphine, especially as availability of the medications has increased.
Methods: As a requirement for approval, the distributor was required to institute a risk management plan that included postmarketing surveillance conducted by an independent contractor. As part of it, applicants to treatment programs were interviewed about whether they had heard of Suboxone, knew anyone who used it including to get high, and whether they knew of street sales. The same questions were asked about other drugs as comparators. Weighted responses were summed for each product to create an abuse scale termed Mean Abuse Rating (MAR, ranging from 1 to 12). 19,486 interviews were completed from 2004 to 2009. Availability of Suboxone was indicated by the number of tablets distributed
Results: Over 90% of the prescriptions written by physicians for buprenorphine were for Suboxone and its availability has increased 1,651% since 2005. The MAR for Suboxone increased over time from 1.6 in 2004 to 4.5 in 2009. It has remained significantly lower than positive comparator drugs such as OxyContin (8.9 to 9.3), oxycodone (7.2 to 8.2), Vicodin (8.3 to 8.7), methadone (8.1 to 7.3) and heroin (9.3 to 8.8). By 2009, 21% of the applicants were aware of its use to get high and 33% were aware that Suboxone was sold on the street
Conclusions: Applicants to substance abuse treatment programs are aware of diversion and abuse of Suboxone, and this awareness has steadily increased over time. However, in relationship to increases in the availability of Suboxone, the increases are small. Nevertheless the increases merit continued monitoring and the development of strategies to curtail diversion and abuse.
Financial Support: This research was supported by a contract from Reckitt Benckiser Pharmaceuticals, Inc to CRS Associates.

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DESIGN CONSIDERATIONS FOR INTERACTIVE VIDEO INTERVENTIONS ON MOBILE DEVICES.

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Aims: Develop an implementation model to improve the reach and effectiveness of video interventions in clinical settings.
Methods: Brief video interventions delivered on handheld computers can help reach patients who otherwise might be missed. Video, however, does not in itself make interventions successful - presentations need to be designed and evaluated for particular settings and populations. The following design considerations, derived from a successful intervention and clinical trial (Aronson and Bania, in press), can be applied to SBIRT protocols for HIV, drug use, and other public health issues in clinical settings where demand may outstrip resources.
Recommendations:
Use a mobile computer: Instead of screening videos for groups on a large television like-monitor, individually deliver video segments to each client on handheld computers. Not only does this assure a greater degree of privacy, but it allows the selection of videos more contextually anchored to clients' drug use patterns, e.g., separate components of a video can be delivered to address hazardous drinking, prescription drug abuse, injection risk behavior.
Integrate data collection with video delivery: Computers can be programmed to quantify cognitive, attitudinal, and behavioral responses to video interventions, eliminating the need for paper evaluation forms and delays and errors associated with key punching data.
Keep interventions brief: Short videos and computer-based screening enable implementation in the main treatment areas of a facility, where volume and need may be greatest.
Compare multiple approaches: Computers can randomize participants to see different videos based on competing theories of multimedia learning. The comparative effectiveness of each video can then be quantified automatically.
Conclusions: Emergency departments and other high volume clinical settings provide important points of contact for hidden and vulnerable populations, e.g., users of illicit drugs, sex workers, and homeless persons. Optimized, computer-based video interventions can increase the number of patients screened, and more effectively reach those most at risk.
Financial Support: NIDA (5T32 DA07233)

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COCAINE-INDUCED CHANGES IN PREFRONTAL CORTEX GLUTAMATE RECEPTOR EXPRESSION DEPEND UPON HOMER1 AND HOMER2 PROTEINS.

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Aims: Homer1b/c and Homer2a/b are glutamate-associated scaffolding proteins that actively regulate behavioral sensitivity to cocaine. We have previously reported that long-term (3 weeks) withdrawal from a sensitizing cocaine injection regimen elevates prefrontal cortex (PFC) expression of Homer2a/b, concomitant with increases in mGluR1 and NR2b expression. The present study tested the hypothesis that if the cocaine-induced increase in PFC Homer2 expression contributed to up-regulated glutamate receptor signaling within this structure, then these proteonomic adaptations should be absent in Homer2 null mutant mice.
Methods: To test this hypothesis, Homer1 knock-out (KO), Homer2 KO and their respectively wild-type (WT) controls were treated repeatedly with either saline or 30 mg/kg cocaine for 7 days. Three weeks later, PFC tissue was dissected out and processed by immunoblotting for the levels of Homers, mGluR1/5, and NR2a/b.
Results: As reported previously, WT mice exhibited cocaine-induced increases in PFC Homer2a/b, mGluR1 and NR2b expression. Homer1 KOs did not differ from WT mice regarding basal PFC protein expression or cocaine-induced glutamate receptor changes. However, Homer1 KOs failed to exhibit a cocaine-induced rise in Homer2a/b expression. In contrast, Homer2 KO mice exhibited lower PFC levels of mGluR1 and NR2b and failed to exhibit a cocaine-induced increase in either of these receptors.
Conclusions: These data indicate the importance of a balance between Homer1b/c and Homer2a/b expression for maintaining normal basal mGluR1 and NR2b expression, as well as for cocaine-induced increases in the expression of these receptors during protracted withdrawal.
Financial Support: NIDA grant DA024038 to KKS and NRSA to AWA

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DOPAMINE TRANSPORTER, SUBSTANCE ABUSE, AND SEX DIFFERENCES IN NOVELTY-SEEKING.

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Aims: Dopamine (DA) influences the regulation of motivation and reward, which are associated with personality (novelty-seeking; NS) and substance abuse. Variation in genes that regulate DA transmission (DAT) are associated with personality and substance abuse, but few studies have examined sex differences.
Methods: We examined variation in 3 single-nucleotide polymorphisms (SNPs) in DAT (rs27072, rs460000, rs6347) across a sample of cocaine-dependent individuals (n=114; 50 female) and healthy controls (n=73; 40 female). Chi-square analyses and between-subjects ANOVA analyses with NS from TPQ as the dependent variable was examined with group (cocaine vs control), gender, and 3 SNPs as between-subject factors were conducted. Main effects and 2-way group × DAT, gender × DAT, and gender × group interactions were included.
Results: For rs6347, females were more likely to have AG or GG alleles ($p<.05$). No gender differences were observed for other SNPs. For rs27072, cocaine patients were more likely to be homozygous (CC) ($p=.05$). For the NS ANOVA, cocaine patients had higher NS scores than controls ($p<.01$). There was a main effect for rs27072 ($p<.05$) with the CT or TT genotype reporting higher NS scores than the CC genotype. There were significant gender interactions for rs27072 and rs6347 (p's<.05). For both SNPs, males with at least one rare allele had higher NS scores (p's<.05) and there were no genotype effects for females. There was a marginal group × rs27072 interaction ($p=.08$) with cocaine patients where the CT or TT genotype had higher NS scores than those with CC ($p<.05$), and there was no genotype effect for controls, $p=.8$. There were no effects for rs460000.
Conclusions: Data suggest that DAT variation may play a role in risk for cocaine dependence and may be related to NS, particularly among males. Although results should be interpreted cautiously, findings suggest that other DA regulation genes may influence NS in females (e.g., COMT). Future work will examine sex differences in COMT and its role in substance abuse and NS.
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ENSURING QUALITY DRUG TREATMENT FOR CRIMINAL JUSTICE CLIENTS: STAFF'S ATTITUDES TOWARD MANDATED CLIENTS.

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Aims: In recent years, there has been a substantial increase in the number of clients entering drug treatment through the CJ system. With the Drug Law Reform, in NYS between 10/09 and 6/10 there were 5,143 CJ admissions to residential treatment which was 406 more compared to the same time period in 08-09 (excludes DWI) and 39,890 CJ admissions to outpatient, an increase of 1,167. Sadly, addiction staff receive little or no training on how to address the specific needs of these clients. Past research has shown that staff's attitudes of clients have a strong impact on client's treatment retention and post treatment outcomes. Yet there are few, if any, studies examining addiction staff's attitudes toward CJ mandated clients. To close this gap, this project examined addiction staff's attitudes toward mandated clients and the relationship between attitudes and client retention.
Methods: A 20 item attitude scale was developed and using pilot data item analysis indicated it was reliable (α =.86).The scale was administered to 110 treatment staff in 7 long-term residential and 1 outpatient program in NY.
Results: Findings indicate staff have equally positive attitudes toward mandated and voluntary clients. Over half (63%) of the staff feel there is really no difference between mandated and voluntary clients and 82% believe mandated clients are as likely to understand their addiction as other clients. However, 37% of the staff feel mandated clients are not serious about their treatment and 25% feel they create trouble in the program. Additionally, findings indicate that programs with larger numbers of mandated clients had more negative staff attitudes. Preliminary analysis examining the relationship between staff attitudes and client retention revealed programs with more positive attitudes had higher retention rates among mandated clients.
Conclusions: Based on the findings, it is important to help staff diminish negative attitudes toward mandated clients in order to ensure quality treatment for these CJ clients.
Financial Support: There was no financial support for this project

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PATTERNS OF MEMORY IMPAIRMENTS IN A SAMPLE OF ACTIVE HEROIN USERS IN PENANG, MALAYSIA.

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Aims: While cognitive functioning is essential for a beneficial participation in treatment and other interventional programs, cognitive impairments are prevalent in long term drug users. To explore patterns of potential cognitive impairments in long term heroin users in Malaysia, we are conducting a study to evaluate broad range of neurocognitive functions in this population. This brief report outlines patterns of memory impairments identified using the Rey-Osterrieth Complex Figure (ROCF) test in forty active heroin users in Penang, Malaysia

Methods: All participants were males aged 20 -60 years. 34/40(85%) of participants had more than five years of drug use history and 28/40(70%) of them were injectors. All urine samples collected in this group were positive for opiate metabolites and 21/40 of them also were positive for other drugs, including ATS, THC, Methadone and Benzodiazepines.

The cognitive tests were performed at least several hours after the most recent drug use and participants were not intoxicated or visibly impaired during the tests. We evaluated memory performance using 6 summary scores for the ROCF test using Boston Qualitative Scoring System.

Results: 16/40 (40%) of the participants showed no memory impairments and were in average or above average range of scores. 24/40 (60%) of the participants had impairments ranging from mild to severe in at least one summary score. In those who had memory impairments, 1/40 (2.5%) showed severe impairment in five domains, 6/40 (15%) had moderate to severe memory impairment in at least one score, and 21/40 (52.5%) showed mild impairment in at least one score.

Conclusions: Most frequent impairments in this sample, 14/40 (35%), were in the ROCF subscales related to short-term or immediate memory performance. We are currently also collecting the same data from a sample of matched non-drug users in Penang, Malaysia.

Financial Support: Ministry of Science, Technology and Innovation Malaysia

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CLINICAL CORRELATES OF SPONTANEOUS WITHDRAWAL FROM PRESCRIPTION OPIOIDS.

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Aims: Chronic pain, depressive disorders and nicotine dependence are prevalent among opioid-dependent adults. The purpose of this study was to evaluate the relationship between opioid withdrawal severity and bodily pain, depressive symptoms, cigarette smoking and nicotine withdrawal.

Methods: Adult smokers dependent on prescription opioids were enrolled in an ongoing clinical trial examining a novel treatment for opioid withdrawal. This study examined data from the first 7 days of opioid detoxification (n=14). Subjects completed daily assessments including the McGill Pain Inventory (MPI), the Beck Depression Inventory (BDI), cigarette craving (Brief Questionnaire of Smoking Urges [QSU]), nicotine withdrawal (a modified Minnesota Nicotine Withdrawal Scale [MNWS]) and subjective ratings of opioid withdrawal. Observer ratings of opioid withdrawal, physiological measures and number of cigarettes smoked were also collected. Correlation analyses were conducted using Pearson coefficients.

Results: Subjective and observer ratings of opioid withdrawal severity were positively correlated with scores on the MPI and BDI ($p<.05$). The QSU and modified MNWS were also significantly correlated with opioid withdrawal severity ($p <.05$); however, no association was detected between opioid withdrawal and number of cigarettes smoked per day.

Conclusions: As the study excluded those with significant medical or psychiatric comorbidity (other than drug use), it appears that pain and depressive symptoms were due to opioid withdrawal. While nicotine withdrawal and cigarette craving were positively correlated with opioid withdrawal severity, smoking behavior was not associated with opioid withdrawal. The relationship between opioid and nicotine withdrawal cannot be readily established, as ratings of each syndrome share common symptoms (e.g., anxiety, insomnia). Thus, current methods of nicotine withdrawal assessment may lack specificity in the context of opioid withdrawal.

Financial Support: R01 DA027068 (MRL), T32 DA007304, UK Clinical Operations and Development Center

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REACTIVITY TO LABORATORY-INDUCED STRESS AMONG INDIVIDUALS WITH PRESCRIPTION OPIOID DEPENDENCE.

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Aims: Elevated levels of stress reactivity have been associated with use and relapse to drugs of abuse. Little is known, however, about stress reactivity among individuals with prescription opioid dependence. The current study aimed to prospectively investigate reactivity to a standardized, laboratory stress provocation among individuals with prescription opioid dependence as compared to a control group.

Methods: Participants were 55 individuals with current prescription opioid dependence or healthy controls who were admitted for an overnight hospital stay, followed by an inpatient test day during which they completed the Trier Social Stress Task (TSST). Immediately prior to and following the TSST, we assessed subjective responses, dehydroepiandrosterone (DHEA), cortisol, and physiological responses. Coping strategies were assessed immediately following the task.

Results: In comparison to controls, prescription opioid-dependent individuals evidenced significantly higher basal subjective stress, anxiety, anger, and sadness, as well as systolic and diastolic blood pressure. Prescription opioid-dependent individuals were more vulnerable to the stress provocation, as evidenced by more pronounced subjective stress and DHEA responses, and a reliance on emotion-focused as compared to task-focused coping.

Conclusions: The findings demonstrate the utility of laboratory stress provocations among individuals with prescription opioid dependence. The increased sensitivity to stress observed among individuals with prescription opioid dependence suggest that pharmacological and behavioral interventions aimed at dampening stress reactivity and strengthening task-oriented coping may assist in treatment and relapse prevention efforts. Recruitment is on-going and the findings presented will report on the full sample.

Financial Support: K23 DA021228 (Back, S); 5 UL1 RR029882 (Brady)

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PHARMACOKINETICS OF ORAL 3,4-METHYLENEDIOXYAMPHETAMINE IN HUMANS.

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Aims: MDA is an illicitly use drug that is sometimes considered an analog of MDMA (3,4-methylenedioxymethamphetamine, "ecstasy"). In vivo, MDMA is N-demethylated to MDA, which is itself metabolized to 4-hydroxy-3-methoxyamphetamine (HMA). Knowledge of MDA and HMA kinetics in humans is limited to data from MDMA administration studies where low formation of these compounds likely leads to inaccurate parameter estimation. We sought to measure their pharmacokinetics after a single oral dose of MDA in humans in a controlled setting.

Methods: In a placebo-controlled, double-blind, within-subjects study, 12 individuals received a single 98 mg per 70 kg body weight dose of MDA. Blood and urine were collected at scheduled intervals for analysis of MDA and HMA by GC/MS.

Results: MDA was well-tolerated by all participants (11 M/1F; five with prior MDA use, 12 with prior MDMA and hallucinogen use). Cmax and AUC 0-∞ for MDA were 229 ± 39 ng/mL (mean ± SD) and 3636 ± 958 for MDA and 92 ± 61 ng/mL and 1544 ± 741 for the metabolite HMA. Total MDA clearance was 30267 ± 8214 mL/min. There was considerable between-subject variation in metabolite exposure: HMA C max and AUC varied over 7-fold and 4-fold, respectively, between the highest and lowest individuals.

Conclusions: Pharmacokinetics of MDA resemble those of an iso-molar dose of MDMA, suggesting differences in duration of acute effects between MDA and MDMA are not due to kinetic differences.

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COLLEGIATE RECOVERY COMMUNITIES: STUDENT MEMBERSHIP AND PROSPECTIVE OUTCOMES.

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Aims: The high prevalence of substance use on college campuses poses a real threat to students in recovery and an obstacle to pursuing a degree for young people with substance use disorders. Collegiate Recovery Communities (CRC) are a campus based peer driven model of ongoing comprehensive recovery support that creates a culture of recovery; 8 universities have a CRC, others are in planning stages. The lack of data on the population served and their outcomes hinders the adoption of the CRC model. We (1) Describe the CRC student membership and (2) Present the first prospective CRC outcome data on substance use and functioning at 6-months post intake.
Methods: Students (N=148) recruited at 5 CRCs in the South and Midwest in Fall 2010 will be reinterviewed 6 months later using standardized scales (e. g., GAIN, MOS, WHOQOL-BREF). Abstract on baseline only, expected prospective cohort N = 125 in June 2011.
Results: CRC students are 52% male, 88% White, median age 24.8 years. Median duration of alcohol/drug abstinence is 24 months, median CRC enrollment, 3 semesters. Over half would not have enrolled at current institution had there not been a recovery program. Students have an extensive history of polysubstance use starting in early teens with 90% citing drugs as primary or secondary problem and 88% alcohol; 90% received addiction treatment, 88% treatment for emotional problems, 89% rate their past substance use as very/extremely harmful to their lives and perceive potential relapse as highly harmful as well. They report multiple current recovery activities and sources of recovery support including 12 step (86%), CRC members and staff (66%), doing community service (46%), and therapy (31%). Perceived recovery support, satisfaction with life, with self and with available supports are very high.
Conclusions: CRCs serve young adults with severe substance use problems who are maintaining their sobriety while pursuing an education by relying on multiple sources of peer and professional support. Additional research is needed to inform relapse prevention programs on campus.
Financial Support: HRSA D1DHP20055A0

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EATING A HIGH FAT CHOW DIFFERENTIALLY AFFECTS SENSITIVITY OF ADOLESCENT MALE AND FEMALE RATS TO COCAINE-INDUCED LOCOMOTOR ACTIVITY.

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Aims: Several factors impact the behavioral effects of drugs acting on dopamine systems. For example, after just 1 week of eating high fat chow, male adolescent, but not male adult, rats are more sensitive to the locomotor stimulating effects of cocaine as compared with rats eating standard chow. This study examined whether eating high fat chow during adolescence or adulthood modifies sensitivity of female rats to the locomotor effects of cocaine (1.0-17.8 mg/kg).
Methods: Separate groups of Sprague Dawley rats (PND 25 or 75) had free access to standard (5.7% fat) or high fat (34.3% fat) chow, or restricted access to high fat chow (body weight matched to rats eating standard chow).
Results: In female adolescent rats with restricted access to high fat chow for 2 weeks, there was a non-significant trend for increased locomotor effects of cocaine, compared to adolescent rats with free access to either standard or high fat chow. Eating high fat chow for 2 weeks did not markedly affect sensitivity of female adult rats to cocaine.
Conclusions: These data suggest that the effect of eating high fat chow on sensitivity to cocaine is significantly greater in male adolescent, than in female adolescent, rats. Taken together, adolescence in males might represent a critical period when eating high fat foods influence sensitivity to, and possibly vulnerability to abuse, cocaine or other related drugs.
Financial Support: CPF is supported by Senior Scientist Award DA17918.

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ASSOCIATIONS OF WOMEN'S COPING RESOURCES WITH LIFETIME MARIJUANA USE AND ALCOHOL ABUSE ACROSS RACIAL ETHNIC GROUPS: RESULTS FROM A NATIONAL SURVEY.

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Aims: We estimate prevalence of licit and illicit substance use and abuse across different income levels for women identifying with various racial-ethnic groups and examine differences in associations of coping resources with substance use and abuse for women in each group.
Methods: Phenotypes used are lifetime use and abuse for marijuana, and alcohol abuse and dependence. Predictors include ethnicity (African American, Caucasian, Hispanic), SES (income) and other individual and personal resources such as resilience and social support. We examine the relationships of these predictors to substance measures for the women who were interviewed as part of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Wave 2 dataset (N = 20,089). We supplemented Wave 2 data, which has measures of individual and personal resources with relevant Wave 1 items to construct lifetime use and diagnostic phenotypes. This dataset was used because of it large size and availability of DSM-IV diagnostic criteria. We performed logistic regression analysis to examine the effects of race-ethnic background, income, resilience and social support on these phenotypes controlling for age.
Results: Our preliminary findings of un-weighted data show that, across various ethnic groups, diagnosis of alcohol abuse or dependence and marijuana use are more prevalent at higher income levels. For Caucasian women and African American women greater resilience was associated with lower lifetime use. For Hispanic-Latina women, presence of social support was associated with increased use.
Conclusions: Our results point to the association of different social and personal resources with prevalence of alcohol and marijuana use in various racial-ethnic populations. Further analyses will include accurate race-weighted analysis and variance estimates (including treatment of multiple races); examine why different resources are salient to different groups; and expand analyses to compare with men's patterns.
Financial Support: R01DA20922 and T32DA07313

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SUBJECTIVE SLEEP QUALITY IN OPIATE-DEPENDENT SUBJECTS IN METHADONE AND BUPRENORPHINE MAINTENANCE TREATMENT.

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Aims: Although sleep disorders are frequent complaints in opiate-dependent subjects, only few studies have examined the subjective sleep quality among opiate-dependent patients in treatment. Moreover, these were cross-sectional studies and could not examine the evolution of sleep quality throughout treatment.
Objective: 1) To describe subjective sleep quality at intake and 12 months later and sleep quality evolution in opiate-dependent subjects in methadone and buprenorphine maintenance treatment, 2) To determine factors associated with sleep quality at intake and 12 months later.
Methods: Patients continuously in methadone or buprenorphine maintenance treatment for 12-month were included in this study. Subjects were assessed with ASI, MINI, BAI and BDI. The Sleep section of the Nottingham Health Profile assessed subjective sleep quality.
Results: 149 patients (72% males, 32 y.o.), treated by methadone (58%) and buprenorphine (42%) were included. Results showed an altered sleep quality at intake, a significant improvement at 12-month but sleep quality was still altered in comparison to literature controls. Three groups were defined: 56% reported an improvement of their sleep quality, 25% a deterioration and 19% no change. Sleep quality was not associated with substance use neither at intake nor at 12-month but was highly associated with psychological status both at intake and 12-month.
Conclusions: There is a need to better characterize the sleep disorders and to better qualify the three groups of evolution of sleep quality by coupling subjective and objective measures of sleep.
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PATTERNS OF RECREATIONAL USE OF GBL, IMPACT ON PREVENTION POLICY - IN SITU SURVEY.

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Aims: In situ cross-sectional survey to approach the phenomenon of GBL use, measure prevalence of use in a sample of dance clubs clients in Paris, identify profiles and risk factors of use to determine the targets of prevention policy, measure the impact of prevention messages and their possible limits
Methods: Our study was carried out in party scene among 410 clubbers in Paris in 2009-2010. Respondents were recruited at random at their arrival in seven clubs: 370 agreed to answer a 15-items questionnaire
Results: Prevalence of use is high: 22.4% (n = 83) especially among men (30,5% vs. 9,6%, p<0,0001), youngsters (32,7% of users among respondents < 20 yo ; 41,5% of users are < 20 yo, 54,9 % < 25 yo) and gay (47,5% versus 13,9%, p<0,0001 ; 57,3% of users and 73.3% of frequent users are gay). 13,4% of consumers report using GBL «only once», 39% "occasionally" and 47,6% "frequently". GBL is not only a party-drug even if 99% of users consume in clubs and 9.3% at home, 45.8% of frequent users consume at home (40% are < 20 yo). Users of GBL have already mixed GBL with other drugs : Cocaine (89%), MDMA (72,8%), Ketamine (48,8%) and - the most risky in the short term - alcohol (41,5%). Only 14.7% of respondents (regardless of status of use) are sensitive to prevention messages and 14.6% of users say that prevention policy has an impact on their habits: 2.9% believing that these messages are shoddy, 24.3% not feeling concerned, 72,8% not wanting to know the risks or don't care. 73% of respondents and 34,6% of users believe that one can become addicted to GBL (p<0,001). The occurrence of adverse events (overdose or sickness) during the use does not affect users' opinions about the product (80%) and does not affect their consumption (90%).
Conclusions: There is a strong link between GBL and sexual orientation and age. Young gay men "clubbers" are more exposed to dangers of GBL by the high frequency of use, the total disregard of the product and especially risky associations. GBL does not scare users because having experienced adverse events doesn't change patterns of use. Prevention messages, when received, don't seem to reach their target
Financial Support: none

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THC IMPAIRS, AND AMPHETAMINE FACILITATES, MEMORY ENCODING PREFERENTIALLY FOR EMOTIONALLY SALIENT STIMULI.

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Aims: Emerging theories suggest that drug addiction is a disorder of memory, and several drugs of abuse act directly on brain regions involved in emotional memory. Thus, these drugs may alter memory encoding of emotional events surrounding drug use episodes. The effects of drugs on memory may vary across drug types, and they may be related to the drugs' effects on mood. In this study, we examined the effects of two drugs of abuse on encoding of emotional material: 1) Δ^9-tetrahydrocannabinol (THC) – a drug with mixed effects on mood that is known to impair memory; and 2) d-amphetamine (AMP) – a drug that produces positive mood states and enhances cognitive performance.
Methods: Two studies were conducted - one with THC (N=25) and one with AMP (N=25). Healthy volunteers (18-35yrs) received placebo and 2 doses of either THC (7.5 & 15 mg) or AMP (10 & 20 mg) p.o., randomized across three study sessions. Ninety minutes after dosing, they viewed novel pleasant, neutral, and unpleasant pictures. Sober recognition memory accuracy was assessed 2 days after each study session. Subjective drug and mood, and physiological effects were recorded at regular intervals and examined in relation to drug-induced alterations of memory encoding.
Results: Given prior to encoding, AMP improved, whereas THC impaired, subsequent, sober recognition memory for emotionally-salient pictures. These effects on memory were limited to positively- and negatively-valenced pictures, and neither drug affected memory for pictures of neutral valence. There was no apparent relationship between the drugs' effects on memory and their effects on mood state or physiology.
Conclusions: Consistent with their actions on brain regions involved in emotional memory, drugs of abuse preferentially affect encoding of emotionally-salient stimuli in humans.
Financial Support: This research was supported by NIDA DA02812 and T32 DA007255.

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EFFECTS OF VOLUNTARY EXERCISE ON TWO MODELS OF MORPHINE WITHDRAWAL.

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Aims: The present study investigated the effects of voluntary exercise on morphine withdrawal following chronic administration.
Methods: Four groups of C57Bl6J mice were used in each experiment: 1) exercise/morphine 2) sedentary/morphine 3) exercise/saline 4) sedentary/saline. Exercise groups were given free access to activity wheels in their home cages during a 1week acquisition phase and during the withdrawal phase. Mice received either saline or 30 mg/kg, (s.c.) of morphine, twice daily for 5.5 days (11 injections). Withdrawal behaviors were measured at 0, 8, 24, 32 and 48 hrs after the final morphine or saline injection as well as at baseline points before and after the exercise acquisition phase. Withdrawal was assessed with two procedures: 1) mice were placed in a 4L beaker and the number of jumps that occurred in 30 min was recorded (n=8) or 2) thermal sensitivity was measured on a hotplate set at 50, 52, 54 and 56 °C (n=4).
Results: Jumping was significantly increased in all groups treated with morphine at 8, 24, and 32 hrs, but not 48hrs after the last morphine injection. Preliminary analysis indicates that withdrawal jumping was not different in mice that had access to activity wheels.
Thermal sensitivity was greater in mice treated with morphine than in saline-treated mice. In the sedentary groups, thermal sensitivity was significantly greater in the morphine group than in the saline group at 24, 32, and 48 hrs after the last morphine injection. In the exercise groups, differences in thermal sensitivity between mice treated with morphine or with saline were apparent only at 24 hrs and, at all points, less than sedentary groups. Within saline groups, thermal sensitivity was greater in the sedentary group as compared to the exercise group at 8, 24, 32 and 48hrs.
Conclusions: Access to activity wheels did not produce a significant decrease in withdrawal jumping following chronic morphine administration; however, access to activity wheels appeared to decrease thermal hypersensitivity under identical conditions.
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SEX DIFFERENCES IN MARIJUANA USE AMONG URBAN AFRICAN-AMERICAN ADOLESCENTS.

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Aims: The aim of this study was to combine toxicological results with self-report data in order to estimate male-female variation in the occurrence of marijuana smoking among urban African American adolescents participating in a longitudinal study of prenatal exposure to cocaine and other drugs.
Methods: This study was conducted in the context of the Miami Prenatal Cocaine Study (MPCS), a longitudinal study of a well-retained cohort of 476 full-term African American prenatally cocaine-exposed (PCE; n=253) and non-cocaine-exposed (NCE; n=223) infants enrolled at birth and followed serially through age 16/17 years. A total of 407 (86%) were seen at least one of the scheduled 12-, 14/15-, or 16/17-year research visits, when marijuana exposure was assessed by confidential self-report as well as urine and hair assays. United States Drug Testing Laboratory in Des Plaines, IL performed ELISA screen of urine and hair for cannibinoids with confirmation by gas chromatography/mass spectroscopy. Odds ratio estimates of the male-female variation (OR) are from the generalized linear model with generalized estimating equations.
Results: There was marked male-female variation in occurrence of marijuana smoking by mid-adolescence (males, 40%; females, 11%; p<0.05). Estimated across all study visits, this association is moderately strong and statistically robust (OR = 4.4; p<0.05). PCE was not associated with marijuana smoking (p>0.05) and did not appear to modify the male-female variation (product-term p>0.05). As to the value of the toxicological assays, of the 92 marijuana-positives observed at age 16/17 years, 25 had negative self-report with positive urine or hair results.
Conclusions: Within an urban African American cohort, we observed marked male-female variation in the occurrence of marijuana smoking by mid-adolescence. We note the value of strengthening confidential self-report assessments with toxicological assays.
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PSYCHIATRIC COMORBIDITIES AS A FUNCTION OF SUBSTANCE TYPE AND GENDER WITHIN RESIDENTIAL SUBSTANCE USE TREATMENT.

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Aims: Elevated rates of psychiatric disorders are found among individuals with substance use disorders, however, little research examines these rates within residential settings. The current study aimed to fill this gap by examining rates of psychiatric disorders as a function of gender and substance type within residential treatment. We expected to find elevated rates of psychiatric disorders within this sample, particularly among women. Since the study was exploratory, we did not have a priori hypotheses about disorder rates as a function of substance type.
Methods: 503 patients in residential substance use treatment were administered the Structured Clinical Interview for the DSM-IV and Diagnostic Interview for Personality Disorders. Chi-square tests for categorical variables and ANOVAs for continuous variables were used to examine the significance of group differences in diagnosis rates as a function of gender and substance type.
Results: 60.6% of patients had a current comorbid psychiatric disorder and more than 30% had at least two disorders; rates were significantly lower (27%) among patients without substance dependence. The most common diagnoses were major depressive disorder (25.8%), antisocial and borderline personality disorders (25.3% and 24.2%, respectively), and PTSD (14%). Females were significantly more likely to meet diagnostic criteria for psychiatric disorders than males (73.7% versus 55.4%), with particularly strong differences observed among patients with alcohol dependence; 94% of women and 71.2% of men with alcohol dependence had a comorbid psychiatric disorder ($p<.01$). Among illicit substance users, cannabis-dependent patients had the highest rates of mood disorders (46%), anxiety disorders (42%), and ASPD (40%), while cocaine dependent patients had the highest rates of psychotic symptoms (11.2%).
Conclusions: Comorbid psychiatric disorders are highly prevalent within residential substance use treatment facilities and differ as a function of gender and substance type.
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DEVELOPMENT OF A NATIVE AMERICAN SUBSTANCE ABUSE TREATMENT PROGRAM FOR INMATES IN SOUTH DAKOTA.

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Aims: This study describes an intensive outpatient program (IOP) specifically focused on Native American (NA) needs developed and implemented in South Dakota correctional institutions and compares it to a standard IOP.
Methods: Treatment approach: Both the NA IOP program and the traditional program were offered over eight weeks. The NA program was based on principles drawn from the Red Road approach and the Wellbriety approach. Both start with "Meditations with Native American Elders: The Four Seasons" and emphasize a holistic understanding of living sober life within the NA community. Talking circles and Eagle feathers were used extensively during the eight weeks. A NA adaptation of AA was also part of the NA IOP program.
Questionnaire: South Dakota Health and Human Services personnel within the correctional facilities from which participants were drawn administered surveys to inmates as part of a program evaluation. Data were collected from both inmates enrolled in the Native American treatment program and from those included in the standard substance abuse treatment option. The research team conducted secondary analysis of these data.
Subjects: Almost 700 inmates have completed this program.
Results: Inmates in the NA IOP were significantly better able to understand their recovery process, had more pride in themselves, and were more open to discussing their recovery issues than those in the traditional IOP group.
Conclusions: The Native American treatment program offered by South Dakota Correctional Institutions is a promising substance abuse treatment option for inmates and should be subjected to a complete and searching evaluation.
Financial Support: Substance Abuse and Mental Health Services Administration/Center for Substance Abuse Treatment

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EPIDEMIOLOGICAL EVIDENCE OF AN ALCOHOL DEPENDENCE PROCESS PHENOTYPE OBSERVABLE SOON AFTER DRINKING ONSET.

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Aims: One can trace the natural history of alcohol involvement by working backward from clinically diagnosed and treated cases to the earliest drinking experiences. Here, we apply an epidemiological perspective on an 'alcohol dependence process phenotype,' by looking forward from the first drinking occasion, in evaluation of the hypothesis that Asian-Americans are protected early in the drinking trajectory.
Methods: Data are from the United States (US) 2004-7 National Surveys on Drug Use and Health (NSDUH), designed to yield nationally representative samples of newly incident drinkers among non-institutionalized civilian residents age 12+ years. For 2004-07, the NSDUH sample includes approximately 222,000 subjects, with 16,728 newly incident drinkers, all of whom started drinking within 24 months prior to assessment. Poisson regressions were used to test the Asian-American protection hypothesis.
Results: Drinking persistence and conditional drinking rate estimates are consistent with greater protection (i.e., less persistence and lower drinking rates) for newly incident Asian-American drinkers compared to non-Hispanic Whites ($p=0.024$ for persistence and $p=0.017$ for drinking rate). These associations were not substantially confounded by sex or other variables under study, although (1) male and female newly incident drinkers were equally likely to persist ($p=0.430$) and (2) newly drinking males had a higher drinking rate ($\beta=0.3$; $p<0.001$).
Conclusions: Results support hypothesized protection for US Asian Americans early in the drinking trajectory, and invite new research on mechanisms conferring protection within this short span within 24 months after first drink. Public health strategies for prevention of alcohol problems can give increased attention to determinants of persistence among newly-incident drinkers, and once drinking starts and persists, to potentially separable determinants of conditional drinking rates.
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PREVALENCE OF CHRONIC PAIN AND INTEREST IN PAIN MANAGEMENT AMONG PATIENTS SEEKING OFFICE-BASED BUPRENORPHINE-NALOXONE TREATMENT.

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Aims: While chronic pain complicates the management of patients receiving opioid agonist maintenance treatment, research on the pain experiences of those seeking buprenorphine-naloxone treatment (BNT) is scarce. This study explored the prevalence of chronic pain (i.e., pain lasting at least 3 months), associated substance use, pain treatment history, and interest in pain management among BNT seekers.
Methods: 244 consecutive individuals seeking office-based BNT were evaluated using a self-report measure developed by the authors.
Results: Participants ranged in age from 19 to 62 years ($M = 33.8$, $SD = 10.4$); 68% were men; 84% were white. The majority (72%) reported pain in the past week. Of the 88 participants (36%) with chronic pain, 78% reported receiving prior medical treatment for pain (30% of whom indicated the treatment worked "a lot" or "completely"). Frequently endorsed lifetime treatments for chronic pain were: over-the-counter medications (82%); physician-prescribed opiates (75%); physical therapy (66%); physician-prescribed non-opiate analgesics (57%); chiropractor (54%); prayer (45%); and physician-prescribed benzodiazepines (36%). Among those with chronic pain, lifetime misuse of substances to manage pain included: "somebody else's opiate pain medication" (87%); "more than prescribed opiate medication" (78%); "heroin" (58%); "other street drugs" (56%); "alcohol" (45%); "street methadone" (36%); "somebody else's prescribed benzodiazepine" (34%); and "more than prescribed benzodiazepine" (26%). Of those reporting chronic pain, 89% reported interest in receiving pain treatment in addition to addiction treatment via their BNT provider.
Conclusions: Chronic pain is common among patients seeking BNT and is associated with substance misuse; patients with chronic pain are interested in receiving pain management services along with BNT.
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METHADONE DOSE AND THE QTC INTERVAL: LITTLE CLINICAL RELEVANCE BIG UNKNOWNS.

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Aims: Methadone is associated with QT prolongation. A QTc ≥ 500 msec may increase the risk for sudden cardiac death. The purpose of this study was to evaluate the dose relationship between methadone and QTc and identify characteristics associated with QTc prolongation.
Methods: All admissions to a single methadone program from 1994 to 2009 were reviewed for record of an ECG. Of 1204 consecutive admissions (representing 778 individuals), 29 had no ECG and were excluded. Of the remaining 749 patients, 403 had an ECG while off methadone (OFF), 346 had an ECG on methadone (ON), and 210 had ECGs both ON and OFF. Demographics, setting of ECG acquisition, and methadone dose were included in a multiple regression analysis of QTc.
Results: Subjects ON were older (mean 46.7 years) v OFF (mean 41.5 years), p<0.05. Mean methadone dose ON was 75.5 mg (SD 32.6). QTc ON was longer than OFF, 439 msec (SD 36) v 423 msec (SD 33), p<0.05. A QTc ≥ 500 msec was noted in 4% ON and 1.2% OFF, p<0.05. In subjects with ECGs both ON and OFF, the QTc was longer ON (440 msec, SD 35) v OFF (429 msec, SD 34), p<0.05. In this group, 4.8% ON and 1.9% OFF had a QTc ≥ 500 msec, p=ns. Three of ten subjects with QTc ≥ 500 msec ON were also ≥ 500 msec OFF. The dose relationship to QTc was significant (p<0.005), with each 1 mg increase in methadone predicting a 0.21 msec increase in QTc. The best regression model of QTc included gender, age, and methadone dose, p<0.005 R^2=0.046 (controlled for the other variables, R^2 for dose = 0.02).
Conclusions: Patients have a longer QTc while on methadone than off methadone. Less than 5% of patients have QTc ≥ 500 msec. The dose relationship to QTc is weak, explaining only 2% of variability. Other variables contributing to QTc prolongation in methadone patients need to be identified.
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REVERSIBLE AND CELL-TYPE SPECIFIC IN VIVO SILENCING OF CNS NEURONS USING IVERMECTIN-GATED CHLORIDE CHANNELS.

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Aims: Significant efforts have been made to develop genetic tools to achieve reversible, in vivo silencing of neurons in awake, freely behaving animals. The goal is to help establish a causal relationship between the activity of specific neurons (or neuronal populations) and behavioral and physiological outcomes. Optogenetics has distinct limitations, including limited utility for longer time-constant neurobiological processes, and invasive instrumentation. Here we describe a novel tool that permits the long-term, but reversible silencing of neurons in a cell-type specific manner.
Methods: We have generated recombinant adeno-associated viral (AAV) FLEX constructs containing a heteromeric ivermectin-gated chloride channel (IVM). The FLEX cassette confers Cre-recombinase sensitive selectivity with virtually no leakage of the transgene. We can take advantage of the availability of the large number of transgenic mice in which Cre is expressed under a specific cell promoter to achieve selective, reversible in vivo silencing of specific neuronal populations. For example, once introduced into the brain of a cre-expressor mouse, administration (i.p.) of the IVM channel ligand will electrically silence the neurons expressing ivermectin channels. Furthermore, we can easily adapt this technique for rat models by co-injection with cre viruses.
Results: In vitro testing in cre-293 cells has verified cre-dependent inversion and cell-surface expression of the IVM channel. We have also placed small unilateral injections of IVM-AAV into discrete areas of the brain, including the midbrain of DAT-cre mice. Co-administration of the IVM ligand (ivomec) and methamphetamine resulted in pronounced circling behaviors compared to baseline, ivomec and methamphetamine only controls.
Conclusions: Using the FLEX-IVM-AAV we can reversibly silence dopaminergic neurons in awake and freely moving animals for hours or days, providing an alternative genetic approach for studying these pathways in behavioral models.
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REGION-SPECIFIC CHANGES IN ZIF268 MRNA FOLLOWING COCAINE SELF-ADMINISTRATION, ABSTINENCE, AND EXTINCTION TRAINING.

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Aims: Repeated drug use is thought to induce neuroadaptations that are associated with behavioral phenotypes of addiction. Non-drug periods, such as abstinence and extinction training, also induce neuronal modifications that may be related to drug craving and the formation of new CS-no US memories, respectively. Previous research has shown that expression of the immediate early gene zif268 is modified by cocaine administration and drug-paired CS presentation. This experiment examined whether zif268 expression is altered by cocaine self-administration, abstinence, and/or extinction training.
Methods: Rats were either trained to self-administer cocaine or received yoked saline administration. They were then euthanized 1 h after either their last self-administration session or after 1, 3, or 20 days of extinction training or abstinence. Zif268 mRNA was measured using in situ hybridization histochemistry with regional autoradiographic quantification.
Results: Consistent with previous research, we found that cocaine self-administration resulted in a down-regulation of zif268 mRNA in the nucleus accumbens core (NACc) relative to saline-yoked controls. Following abstinence, zif268 was up-regulated in the Cg2 region of the anterior cingulate cortex (CG2) and NACc compared to the cocaine self-administration only group. Extinction training up-regulated zif268 in the orbitofrontal cortex and CG2, and increased expression on days 1 and 20 of extinction in both the NACc and nucleus accumbens shell.
Conclusions: While the abstinence effects may be related to the increase in motivation for cocaine that emerges during the course of non-drug periods, the effects found in the extinction groups may be related to different phases of learning and memory taking place during extinction. These findings add to a growing literature on the neural circuitry involved in cocaine abstinence and extinction of cocaine-associated stimuli.
Financial Support: DA11064

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NALTREXONE EFFECTS ON CANNABIS AND COCAINE USE IN ALCOHOL-DEPENDENT PATIENTS WITH SCHIZOPHRENIA: PRELIMINARY ANALYSIS.

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Aims: Naltrexone (NTX) has been shown by our group and others to be effective in reducing alcohol use in patients with schizophrenia. The aim of this report is to assess the efficacy of NTX vs placebo (PLA) in reducing the cannabis and cocaine use in these patients.
Methods: The parent study was a controlled clinical trial of directly-observed NTX vs placebo (PLA) in 90 patients with schizophrenia or schizoaffective disorder and alcohol dependence. This analysis compared the frequency of cannabis and cocaine use in the NTX vs PLA groups over the 12 week course of the study.
Results: Of the 90 subjects, 28(31%) subjects had co-occurring Cannabis Abuse/Dependence and 30(33%) had Cocaine Abuse/Dependence. 44 (49%) reported using cannabis and 29 (32%) reported using cocaine during the baseline 30 days. Baseline urine drug screens were positive for cannabis in 29 subjects(32%) and were positive for cocaine in 24 (27%). Baseline mean frequency of cannabis and cocaine use per 30 days for the entire cohort of 90 were 6.6 (±10.2) and 2.2 (+4.7), respectively. The baseline frequency of cannabis and cocaine use correlated significantly with heavy alcohol use frequency. However, there were no differences in the frequency of cannabis and cocaine use between the NTX and PLA groups over the course of the 12 week study.
Conclusions: Prevalence of non-alcohol SUDs was substantially higher in this sample than in the general population. The baseline frequency of cannabis and cocaine use was significantly related to the amount of alcohol use. NTX did not appear to be effective in reducing cannabis and cocaine use frequency for the sample as a whole, in this cohort of patients with schizophrenia and alcohol dependence. Future investigations should examine the possible interactions between medication assignment and changes in alcohol use on cannabis and cocaine use.
Financial Support: NIAAA R01 AA016355

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DOES TOLERANCE DEVELOP TO THE ANALGESIC, REWARDING AND PRO-EMETIC EFFECTS OF OXYCODONE?

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Aims: Opioids are a treatment of choice in the management of pain. We previously reported that acute oxycodone induces reward and pro-emetic effects at antinociceptive doses. However, opioids are administered chronically for pain management in the clinic. In this study, we determined if the effects seen following acute administration of oxycodone persisted after chronic treatment.
Methods: Adult female Sprague-Dawley rats were administered oxycodone 15 mg/kg by oral gavage for 20 days. Analgesia and pro-emesis behavior were assessed on days 1, 5, 10, 15 and 20. Antinociception was assessed using the hot plate across 6 hr. Pro-emesis was measured via the bedding intake paradigm of pica for 3 hr. Pica is the consumption of non-nutritive substances. Two additional groups of rats also received oxycodone treatment for 20 days. One group was assessed for reward using the conditioned place preference (CPP) paradigm, while the other group was used to determine if withdrawal was present during the CPP testing.
Results: Tolerance to the antinociceptive effects were found only at the later time points. After 10 days of oxycodone, the latency to lick the hind paw had returned to baseline by 3 hr as compared to 6 hr on the first day of treatment. Area under the curve analysis indicated that the magnitude of antinociception decreased by 1-1.5 fold on days 10, 15 and 20.
Similar to the hot plate, tolerance to the pica effects were also seen at the later, but not earlier assessment times.
CPP was still present after 20 days of treatment indicating that tolerance did not develop to the central rewarding effects of oxycodone. Naloxone – precipitated withdrawal was not observed during CPP, so the CPP was not confounded by a conditioned aversion.
Conclusions: In summary, antinociceptive and pro-emetic effects were more sensitive to the development of tolerance, especially in the later stages of drug action. The lack of tolerance to the rewarding effects underscores concerns about abuse potential with chronic oxycodone treatment.
Financial Support: This research was supported in part by USPHS DA018181 from NIDA, NIH.

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IN VIVO NEUROCHEMISTRY OF DESIGNER METHCATHINONE ANALOGS ABUSED BY HUMANS.

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Aims: Despite the widespread abuse of methcathinone analogs, such as 3,4-methylenedioxymethcathinone (methylone) and 4-methylmethcathinone (mephedrone), little information is available regarding the mechanism of these drugs. Here we used in vivo microdialysis in rats to compare neurochemical effects of methylone, mephedrone (+)-methamphetamine (MA) and (+)-3,4-methylenedioxymethamphetamine (MDMA).
Methods: Anesthetized male rats were surgically prepared with jugular catheters and intracranial cannulae aimed at the nucleus accumbens. One week later, in vivo microdialysis was carried out in chambers equipped with photobeams to assess motor activity. Dialysate dopamine (DA) and serotonin (5-HT) were determined by HPLC-ECD. MA, MDMA, methylone and mephedrone were given i.v. at doses of 0.3 and 1 mg/kg.
Results: MA produced large dose-related elevations in dialysate DA, smaller increases in 5-HT, and pronounced locomotor activation. MDMA, methylone and mephedrone produced large dose-related elevations in dialysate 5-HT, with much smaller increases in DA. Methylone and mephedrone were weak locomotor stimulants.
Conclusions: The findings demonstrate that methylone and mephedrone produce elevations in extracellular 5-HT and DA in rat brain that resemble the effects of MDMA. The predominant serotonergic actions of these drugs may reduce their reinforcing properties but enhance their potential for sustained depletions of forebrain 5-HT.
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THE REINFORCING AND DISCRIMINATIVE STIMULUS EFFECTS OF THE (+)-(2S,3S)-HYDROXYMETABOLITE OF BUPROPION IN RHESUS MONKEYS AND MICE.

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Aims: Hydroxybupropion is a major metabolite of bupropion, and its ability to block the DAT and the NET appears to reside in its (+)-(2S,3S)-isomer, which has been in development as an antidepressant (Radafaxine). Based upon PET studies showing sluggish brain kinetics, Volkow and colleagues (2005) suggested that it would unlikely have reinforcing effects, and referred to presumably unpublished preclinical studies showing no self-administration. The aim of this study was to evaluate (+)-(2S,3S)-hydroxybupropion for its self-administration in rhesus monkeys, and for its ability to occasion the cocaine discriminative stimulus in mice.
Methods: Self-Administration: Four rhesus monkeys were trained to lever press reinforced with 0.03 mg/kg i.v. cocaine according to FR50 schedules during daily, 1-h sessions. Subsequently, cocaine was replaced with a dose of (+)-(2S,3S)-hydroxybupropion (0.01-0.56 mg/kg) for 4, consecutive daily sessions followed by progressive ratio tests. Drug Discrimination: Adult male Swiss Webster mice were trained to discriminate 10 mg/kg cocaine from saline during daily (M-F) 15-min sessions reinforced with milk delivery according to FR20 reinforcement schedules. Once training criteria were met, cocaine (0.3-30 mg/kg) and (+)-(2S,3S)-hydroxybupropion (1-30 mg/kg) were tested for their ability to occasion the 10 mg/kg cocaine stimulus.
Results: (+)-(2S,3S)-hydroxybupropion was self-administered by 3 of the 4 monkeys. Break point values ranged from 50 to 400 yielding a mean value of 225 for the group, which was lower than those obtained with bupropion or cocaine. (+)-(2S,3S)-hydroxybupropion (1-30 mg/kg i.p.) occasioned a maximum of 78.7% cocaine lever responding with an ED50 (±CI) of 21.49 mg/kg (15.37-30.04), and dose-dependently reduced response rates with an ED50 (±CI) of 44.36 mg/kg (16.03-122.74).
Conclusions: These results suggest that (2S,3S)-hydroxybupropion may be able to produce subjective effects similar to cocaine and may have an abuse liability, but likely no greater than that of bupropion.
Financial Support: This research was funded by GlaxoSmithKline S.p.A., Verona, Italy.

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STIMULUS CONTROL OF ESCALATED COCAINE INTAKE AND ESCALATION UNDER SHORT ACCESS SESSIONS.

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Aims: A leading preclinical model of drug addiction is the extended access model that yields escalated intake with repeated 6-hr sessions (Ahmed and Koob, 1998). The current studies determined if escalated intake was subject to stimulus control and whether escalated intake could be obtained with a shorter 1-hr session.
Methods: In experiment 1, adult male rats were implanted with chronically indwelling intravenous catheters. Rats were trained to respond on a fixed ratio 1 (FR 1) schedule for food over 5 days. Rats were then trained on a FR 1 for cocaine (0.25 mg/kg/infusion) in 1 hr sessions across 12 days. Finally, rats self-administered cocaine for either 1 or 6 hrs on alternating days over 28 days (14 days of both 1 and 6 hr access). Access conditions were cued by either a dark chamber or house-light, counterbalanced across animals. Experiment 2 was identical to experiment 1, except rats were trained using a 0.1 mg/kg unit dose of cocaine. Experiment 3 was identical to Experiment 2, but access conditions were not cued. In experiment 4, rats were initially trained with 10-min access to cocaine for 12 days. Afterwards, half were maintained on 10-min access and half were switched to 1-hr access for 14 days.
Results: Rats demonstrated escalation only under stimulus conditions that cued extended access. Escalation magnitude was dependent on the cocaine unit dose available, with the 0.25 mg/kg unit dose producing less escalation than 0.1 mg/kg. Rats initially trained on 10-min cocaine access and then switched to 1-hr access also demonstrated an escalation of intake.
Conclusions: The results demonstrate that escalation of cocaine intake is subject to stimulus control, suggesting that the expression of addiction-like behavior can be context dependent, with addictive behavior occurring in one context and not another. In addition, escalation was demonstrated under a short 1-hr session, suggesting that escalation may represent acquisition of a new response pattern due to a change in the access conditions from those used during initial training, rather than specific addiction-like dysregulation of behavior.
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ACUTE STRESS RESPONSE IN MARIJUANA SMOKERS WITH AND WITHOUT PAST TRAUMA EXPOSURE.

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Aims: Trauma exposure is associated with adverse psychological outcomes, including increased drug abuse. A putative mechanism linking trauma and psychopathology is dysregulation of acute stress responding. High trauma rates and altered stress responses have been reported in cocaine users, yet little is known about trauma exposure, stress responses, or the relationship between them in other drug users. We aimed to compare responses to an acute social stressor in marijuana (MJ) users with and without past trauma exposure.
Methods: Non-treatment-seeking daily MJ smokers (20M, 2F) with no current Axis 1 diagnoses (except MJ-related) completed the Trauma Assessment for Adults and the Trier Social Stress Task (TSST), a standardized stressor involving public speaking. Stress response was assessed with heart rate, salivary cortisol, and subjective anxiety (State-Trait Anxiety Inventory; STAI; Profile of Mood States; POMS). Participants also reported drug use and baseline depressive symptoms (Beck Depression Inventory; BDI). Participants were divided into those reporting ≥1 trauma (N=14) and those with no such exposure (N=8). Groups were compared with t-tests. Data collection is ongoing.
Results: Trauma group (TG) participants had been exposed to 3.1 (±1.0) types of trauma. Analyses of existing data indicated that TG had higher BDI scores than the non-trauma group (NTG; p=0.03). TG also had elevated baseline anxiety (STAI: p=0.004; POMS: p=0.008), with no difference in baseline heart rate or cortisol levels. Overall, the TSST increased heart rate and anxiety, with no differences in peak change scores as a function of trauma history. Groups did not differ in current MJ use, but TG started MJ use marginally earlier than NTG (p<0.1).
Conclusions: Trauma did not affect acute stress response. However, even in this homogenous group of regular MJ users without obvious consequences of trauma, trauma exposure was associated with baseline negative affect elevations and marginally earlier onset MJ use. These initial data indicate that trauma exposure, understudied in relation to drug abuse, warrants further study.
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SEVERITY OF PSYCHIATRIC DISORDERS IN TOBACCO USERS.

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Aims: On the one hand, compare prevalence of psychiatric disorders in tobacco users depending on addiction severity; and on the other hand, compare tobacco addiction severity depending on the age of tobacco onset.
Methods: All subjects who went for a tobacco use problem to addiction clinic Bizia, Bayonne between 2006 and 2010 were administrated the Fagerström test and Mini International Neuropsychiatric Interview for DSM-IV (MINI) current and lifetime to determine co-occurring psychiatric disorders.
Results: 189 tobacco users were included: 38.5 % were male and mean age was 44.8 (±11.8) . The Fagerström test showed that 16.4% of patients had no tobacco dependence, 20.1% had a mild dependence, 34.4% had a moderate dependence and 29.1% had a severe or very severe dependence. Subjects who had a severe dependence met more current major depressive episode and more generalized anxiety disorder than the other groups. Mean age of tobacco onset was 16.4 (± 5.1). Subjects with early tobacco onset met more severe tobacco dependence than those with more tardive onset.
Conclusions: The higher severity of tobacco addiction was, the more frequent psychiatric comorbidities were. There is a need for a thorough clinical assessment of psychiatric disorders in subjects seeking treatment for tobacco addiction. Besides, our results support the concept that early tobacco onset leads to a greater severity of tobacco dependence. Selective and indicated prevention strategies should be developed in order to inform about the harms linked to an early onset.
Financial Support: French

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CORRELATES OF POOR HEALTH AMONG RETIRED NFL PLAYERS: A NATIONAL STUDY.

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Aims: Professional athletes, especially NFL players, are in excellent physical health when they sign their first contract. However, many NFL players struggle with poor health after retirement. This investigation examines the factors affecting current poor health of former NFL players.
Methods: A total of 644 former NFL players selected from the 2009 Retired Players Association Directory were interviewed by telephone with the Washington University Survey of Retired NFL Football Players (Cottler et al., 2010).
Results: On average, players were 48 years old (SD =9.2), Caucasian (52%), and played 7.7 years (SD =3.8). Offensive lineman was the most common position played (28%) in the sample. Perception of current health (past 30 days) was dichotomized into "excellent" vs. not. Current and NFL-related factors were evaluated: Demographics, pain and injuries, and misuse of alcohol and opioids. Multivariate logistic regression results with backward elimination indicated that 3+ NFL-related injuries (OR =3.5, 95%CI 1.84-6.69), severe to moderate pain (OR =5.47, 95%CI 1.62-18.45), physical impairment (OR =2.1, 95%CI: 1.12-4.01), and misuse of opioids during NFL (OR =2.6, 95%CI: 1.39-4.89) predicted current lack of excellent health.
Conclusions: There is a greater need for prevention measures to reduce NFL injuries and monitor the use of opioids during NFL play.
Financial Support: (ESPN & NIDA funded, PI Linda B. Cottler, PhD, MPH)

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MANIPULATIONS OF VENTRAL PREFRONTAL CORTEX GROUP1 MGLURS DO NOT AFFECT INCUBATION OF CUE-INDUCED REINSTATEMENT OF COCAINE-SEEKING BEHAVIOR.

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Aims: Exposure to drug-associated cues induces reinstatement of drug-seeking behavior that intensifies with longer withdrawal from drug self-administration, and the ventral prefrontal cortex (vPFC) has been shown to be critical for this phenomenon. Group I metabotropic glutamate receptors (mGluRs) are important for cue-induced reinstatement of cocaine-seeking behavior in animals trained to self-administer drug under limited-access conditions. As we have previously shown a time-dependent reduction in the vPFC expression of the mGluR1 and mGluR5 during withdrawal from extended cocaine access, here we tested whether incubation of cue-induced reinstatement is mediated by functional changes in these receptors within the vPFC.
Methods: Rats lever-pressed for cocaine or saline during 10 daily 6-hr or 1-hr sessions, respectively. To mimic the reduction in Group1 mGluRs, different groups of rats received intra-vPFC injections of the mGluR5 antagonists MTEP (1.5 microgram/side), or MPEP (3 microgram/side), or the mGluR1 antagonist JNJ16259685 (20 nanogram/side) and were tested for cue-induced lever-pressing behavior under extinction conditions at 3 days withdrawal. To overcome the reduction in Group1 mGluRs observed at 30 days withdrawal, in another study, the Group1 mGluR agonist DHPG (27.5 nanogram/side) was infused intra-vPFC immediately prior to testing at 30 days withdrawal.
Results: Despite our previous immunoblotting data, blockade of Group1 mGluRs at 3 days withdrawal failed to affect cocaine-seeking behavior, as did stimulation of these receptors at 30 days withdrawal.
Conclusions: These data suggest that Group1 mGluRs are not directly involved in the incubation of cue-induced reinstatement of cocaine-seeking behavior.
Financial Support: NIDA grant DA024038 to KKS and funds from the UCSB Academic Senate to OBS and KKS.

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FUNCTIONAL INTERACTION BETWEEN HIV-GP120 IN THE BRAIN AND OPIOID MEDICATIONS.

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Aims: Compared to methadone, the most common clinically used opioid medication for pain and opioid dependence management, buprenorphine is a mu-opioid partial agonist, a powerful analgesic in both rodents and humans, has a very long-lasting efficacy, high safety profile and does not possess immunosuppressive properties. The purpose of the present study was to test which of the two opioid medications, buprenorphine or methadone, is the more effective analgesic in the presence of gp120 in the brain.
Methods: Male Sprague-Dawley rats weighing 200-250 g were used, 8-10 rats per group. A sterilized stainless steel C313G cannula guide was implanted into the periaqueductal grey (PAG). The hot-plate test was used to measure the antinociception.
Results: Results:
Buprenorphine and methadone given subcutaneously produced a marked antinociception in the hot-plate test, reaching a peak level of 79 ± 10% and 81 ± 12 %MPA, respectively. Either vehicle (aCSF) or gp120 was microinjected into the PAG before burprenorphine or methadone. The pretreatment with gp120 failed to alter the analgesic effect of buprenorphine, while it was able to diminish significantly methadone-induced antinociception.
Conclusions: Gp120 in the brain differentially interferes with the opioid medications. Buprenorphine is a more effective analgesic in the presence of gp120 in the brain compared to methadone.
Financial Support: DA 06650, DA 13429 and DA 360549.

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FIELDING RESPONDENT-DRIVEN SAMPLING TO STUDY VETERAN REINTEGRATION, MENTAL HEALTH AND SUBSTANCE ABUSE IN THE INNER CITY.

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Aims: AIM: This paper/poster presents the theory, process, and challenges faced in fielding RDS to recruit 300 recent veterans of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) to participate in a five-year panel study. RDS is a particularly valuable procedure because samples obtained in this manner can be used to estimate the characteristics of the target population, in this case all poor veterans returning to New York's low-income neighborhoods in 2011.
Veterans returning to the inner city face elevated risks for substance abuse and mental health disorders. However, the experiences of veterans returning from Iraq and Afghanistan to the city have not yet been studied systematically. The larger study seeks to address this critical information need. The first step in the process is recruiting an appropriate sample. The RDS procedure is particularly appropriate when the target population is highly networked and maintain social relationships. Military veterans who have lived, worked, fought and socialized together through military and veteran's organizations would appear to meet these criteria. To date, RDS has been successfully employed by the Centers for Disease Control to study HIV risk behaviors and others to study injection drug use, sex workers, and jazz musicians. To the best of our knowledge, this study represents the first time this sampling methodology has been employed to study veterans. We provide data on and discuss the detailed procedures we employed covering the major elements and challenges associated with implementing RDS in the field including seed selection, locating and outfitting field sites, managing incentives and coupons, steering the recruitment procedure to meet sample quotas, and site logistics.
Conclusions: We find RDS to be an effective sampling procedure to obtain our target population of veterans in the inner city.
Financial Support: NIAAA, Project #R01 AA020178

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EFFECTS OF ANXIETY AND DEPRESSION ON TREATMENT OF OPIOID DEPENDENCE DURING PREGNANCY.

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Aims: Depression and anxiety commonly co-occur with opioid dependence during pregnancy, but their impact is not clear. This study examined the effects of depression and anxiety symptoms on treatment retention, drug use, and pre-term delivery in opioid-dependent pregnant women. It was hypothesized that reporting symptoms of depression or anxiety at screening would be associated with worse outcomes.
Methods: This secondary data-analysis of a clinical trial of methadone and buprenorphine for opioid dependence during pregnancy used the 15 item Mini International Neuropsychiatric Interview screen to identify symptoms of depression and anxiety.
Results: Of 175 women randomized, 131 completed the study. After controlling for study medication and co-occurring depression or anxiety symptoms, women who reported symptoms of depression at study entry were more likely to remain in the study until delivery (OR=0.38, p=0.02, 95% CI=0.17-0.87), while women who reported symptoms of anxiety were more likely to drop-out (OR=4.50, p<0.01, 95% CI=1.92-10.55). Depression (OR=2.29, p=0.03, 95% CI=1.08-4.85), but not anxiety (OR=1.12, p=0.78, 95% CI=0.53-2.36), was associated with greater likelihood of positive urine screen for illicit drug use during treatment. There was no statistically significant relationship between depression or anxiety symptoms and pre-term delivery.
Conclusions: Identification of symptoms of depression and anxiety is important for ensuring optimal drug-treatment outcomes in opioid-dependent pregnant women.
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EXAMINING THE FACTOR STRUCTURE OF A BEHAVIORAL ECONOMIC DEMAND CURVE MEASURE OF NICOTINE REINFORCEMENT IN ADOLESCENT SMOKERS.

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Aims: The aim of the study is to use exploratory factor analysis to examine the underlying factor structure of the facets of nicotine reinforcement generated from a demand curve measure.
Methods: Participants were 138 adolescent smokers [49% female; age M = 16.5 (SD = 1.21); cigarettes/day M = 5.97 (SD = 5.99)] who participated in a larger study that compared adolescent smokers to a matched sample of nonsmokers on various indices. Nicotine demand curves were generated via a hypothetical cigarette purchase task, which assessed consumption at 26 levels of prices from $0 to $1120 per cigarette. Five facets of demand were generated from the measure [demand intensity, demand elasticity, P (max) (price maximum, or price at which expenditure is maximized), O (max) (output maximum, or maximum financial expenditure on cigarettes), and breakpoint]. Parallel Analysis and Velicer's Minimum Average Partial (MAP) test were used apriori to determine the correct number of components to retain and Principal components analysis was used to examine the latent structure among the variables.
Results: The results revealed a clear two-factor solution: with one factor, including P (max), O (max), and Breakpoint, representing levels of resource allocation; and the second factor, including Demand Intensity and Elasticity, representing levels of consumption relative to price. The two factors were quantitatively distinct.
Conclusions: These findings suggest that nicotine reinforcement as measured via a demand curve is binary in nature, with separate dimensions of resource allocation and consumption. If supported, these findings may contribute to our understanding of adolescents' motivations to smoke and the nature of the reinforcing value of cigarettes.
Financial Support: The study was funded by a grant from the National Institute on Drug Abuse (1RO1DA16737) awarded to Dr. Colby.

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A COMPARISON OF THE REWARDING VALENCES OF STIMULANT TREATMENTS IN ADULT AND ADOLESCENT MICE.

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Aims: Stimulants such as amphetamine (AMPH) are popular treatments for children and adults with ADHD and, more recently, for adult and adolescent childhood cancer survivors with cognitive late effects. Atomoxetine has become a possible alternative medication due to its beneficial therapeutic effects and low abuse liability, especially in more vulnerable populations.
Methods: In this study, conditioned place preference (CPP) was used to compare the rewarding valences of different stimulants among adult (PND 60) and adolescent (PND 35) mice. On Day 1 of CPP, mice were given free access to a three-compartment chamber. The non-preferred side was paired with a dose of AMPH (1, 2, or 4 mg/kg) or atomoxetine (1 or 2 mg/kg) and the preferred side was paired with saline for 6 alternating days. On Day 8, mice were given free access to all chambers for 15 min, and time spent in each compartment was recorded.
Results: Adult mice treated with AMPH showed a significantly greater preference for the compartment paired with 1 and 4 mg/kg, while adolescent mice showed a greater preference for the side paired with 2 and 4 mg/kg. However, no preferences in the adult or adolescent mice were found for either dose of atomoxetine. Compared to the atomoxetine-treated group, mice treated with AMPH spent a significantly greater amount of time on the drug-paired side.
Conclusions: Findings suggest that sensitivity to the reinforcing properties of AMPH may differ between adult and adolescent mice, but overall, preference for AMPH is greater than for atomoxetine. Therefore, atomoxetine may be a preferable option for populations at greater risk for drug abuse if treated with other stimulant medications.
Financial Support: Supported by CA129092 and T32 DA07237.

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ACUTE EFFECTS OF EXERCISE ON RISK-TAKING IN A SAMPLE OF ADOLESCENT MALES.

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Aims: Exercise acutely reduces cravings for tobacco and alcohol, but the mechanism by which exercise impacts these and other risk behaviors is not fully understood. To extend the inquiry into exercise's effects on risk-taking behavior more generally, the current study compared performances on a computer-based risk task after periods of exercise and rest.
Methods: Twenty adolescent males engaged in structured rest and exercise (competitive tennis) conditions. Risk behavior, assessed by the Balloon Analog Risk Task (BART), was measured immediately after each condition, with the order of conditions varied. Repeated-measures analyses compared the main effect of condition and the condition-by-order interaction effect on BART scores.
Results: BART scores indicated significantly greater risk-taking immediately following exercise than after rest . The test of interaction suggested exercise had carryover effects on risk-taking and heart rate.
Conclusions: In this paradigm, exercise's acute effect to reduce desire to engage in substance use did not extend to a reduced impulse to take other risks. This raises the question of the role of participant age, health, and type of risk behavior as potential moderators of the exercise-risk-taking relationship.
Financial Support: This study was conducted as a high school science project and did not have external financial support.

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PREDICTORS OF INJECTION RISK BEHAVIOR AMONG INJECTION DRUG USERS ENROLLED IN THE PHARM-LINK STUDY: A GENDER-STRATIFIED ANALYSIS.

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Aims: Syringe sharing increases HIV risk among injection drug users (IDUs). This analysis examines syringe sharing behavior among IDUs participating in the Pharmacies Making Links to community services (PHARM-Link) study.
Methods: ESAP-registered pharmacies located in areas of high drug activity in New York City were contacted for enrollment. IDUs who purchase syringes at the participating pharmacies were recruited into the study. The analysis studied 595 IDUs, stratified by sex. The sample was 72.1% male (n=429) and 27.9% female (n=166). Receptive and non-receptive sharing behaviors were analyzed separately with logistic regression models.
Results: 20.5% of the men in the sample reported receptive syringe sharing; 27.3% reported non-receptive syringe sharing. After adjustment, increases in both types of sharing were associated with GLB identity, theft or conning, crack smoking, and having at least one usual injection partner. Ease in obtaining new syringes was associated with reductions in both types of sharing.
Among the men, increased non-receptive syringe sharing was also associated with having been stopped by the police while carrying syringes, participation in drug counseling treatment and cocaine injection.
Among the women in the sample, 27.7% reported receptive syringe sharing, and 33.1% reported non-receptive syringe sharing. After adjustment, both types of sharing were associated with GLB identity and having at least one usual injection partner.
Ease in obtaining new syringes and Hispanic race/ethnicity, were associated with reduced receptive sharing. Non-receptive sharing was associated with a high score on a scale that asks about how much trouble drug use causes the participant.
Conclusions: These data support previous findings that syringe access reduces high-risk behaviors. Our results suggest that some groups might benefit from targeted interventions to reduce syringe sharing.
Financial Support: NIDA

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CAFFEINE ALONE AND IN COMBINATION WITH ALCOHOL: PATTERNS OF USE AND ATTITUDES AMONG U.S. COLLEGE STUDENTS.

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Aims: An emerging trend among young adults in the United States is the use of caffeinated energy drinks alone and in combination with alcohol via manufactured (e.g., Four Loko) or individualized (e.g., Red Bull and vodka) mixtures. Despite concerns of adverse health effects associated with consumption of these products, research remains in its infancy.
Methods: The purpose of this convenience survey, therefore, was to assess the patterns of use and attitudes toward caffeinated drinks alone and in combination with alcohol among undergraduate students at Virginia Commonwealth University (VCU; n=886; 65% freshman; 77% < 20 years old; 67% female; 55% white).
Results: Results revealed that 94% of respondents reported past 30-day use of caffeine: soda (66.4%), coffee (48.5%), tea (34.7%), and energy drinks/shots (14.3%). Reasons endorsed for energy drink/shot consumption included "need energy (in general)" (77.4%), "studying" (53.2%), "driving" (30.6%), "drinking them with alcohol while partying" (19.4%), and "before heading out to drink alcohol" (8.1%). Approximately 33% of respondents reported past 30-day use of caffeine/alcohol combination mixtures such as Four Loko (28%), caffeinated soda + any liquor (24%), and Red Bull + any liquor (23%). These respondents stated that they like to consume caffeine with alcohol to "hide the flavor of alcohol" (40%), "drink less and get drunk" (19%), or "stay alert while drinking" (12%).
Conclusions: Overall, results demonstrate that a notable proportion of respondents report use of caffeine and alcohol concurrently, and some respondents may do so to counteract the negative effects of alcohol. Results from this and other work should be used to inform public health campaigns concerning the use of caffeinated drinks alone and in combination with alcohol.
Financial Support: Supported by PHS Grants R01CA103827, R01CA120142, & F31DA028102.

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ALCOHOL AND DRUG USE AMONG HIV-INFECTED DRINKERS IN RUSSIA.

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Aims: Substance use patterns have marked geographic variation with implications for the HIV epidemic. In Russia, substance use has traditionally been perceived to be limited to either alcohol or heroin use. This study characterizes recent polysubstance use among a cohort of HIV-infected Russians reporting recent risky drinking.
Methods: We examined baseline data from the HERMITAGE study, an HIV secondary prevention trial. HIV-infected patients (n=700) reporting risky drinking (NIAAA criteria) and unprotected sex in the past 6 months were recruited from five inpatient and outpatient care sites in Russia from 2007-2010. Use of alcohol and illicit drugs (i.e., heroin, marijuana, sedatives, non-prescription opioids, stimulants) was assessed using CIDI-SF (12 months).
Results: Participants had a median age of 30±5.2 years and were 59 % male. Among this group of HIV-infected individuals with past 6-months risky alcohol use, other substance use in the past year was common: heroin (63%); marijuana (46%); sedatives (32%); non-prescription opioids (33%); and stimulants (31%). Overall 75% reported using at least one other drug in addition to alcohol; proportions reporting use of one; two and three or more substances in addition to alcohol were 14%, 14%, and 46%, respectively. The most common combinations were heroin & alcohol (51%) and marijuana & alcohol (39%).
Conclusions: Drug use, particularly heroin and marijuana, is very common among Russian HIV-infected risky drinkers who report unprotected sex. When addressing HIV prevention and treatment in this region of the world, it is important to recognize that substance use is not limited to alcohol marijuana or heroin alone, but rather polysubstance use is common.
Financial Support: National Institute on Alcohol Abuse and Alcoholism (R01-AA016059)

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EFFECTIVENESS OF TWO-STAGE TRAINING FOR BRIEF INTERVENTIONISTS IN A MULTI-SITE TRIAL.

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Aims: Effective training in psychosocial treatment modalities is critical to maintaining fidelity in both research and practice. Here we evaluate the effectiveness of a two-stage training for interventionists participating in NIDA Clinical Trials Network Study 0047: Screening, Motivational Assessment, Referral, and Treatment in Emergency Departments (SMART-ED).
Methods: Interventionists at the first 2 sites initiating the study received a 2-day training in basic Motivational Interviewing skills, followed 1 week later by a 2-day training in the specific counseling intervention used in the trial. They then completed practice sessions with consenting ED patients. Audiotapes of these sessions were reviewed by an expert rater, using the Motivational Interviewing Treatment Integrity scale (MITI, version 3.1.2) and content checklists. To become certified, interventionists had to score at least 4.0 ("competent") on the 5-point Global Clinician Rating from the MITI and 80% on content checklists, for 2 out of 3 sessions.
Results: Participating interventionists were 5 females and 3 males, average age 36 ± 9, 4 of whom were licensed or certified as counselors, with 2 years mean counseling experience (range 0-7). Their self-reported pre-training understanding of MI was moderate (5.5 mean rating on Likert scale 0-9). All participants met criteria for certification after only 2 practice sessions. All interventionists scored 100% on the content checklists for both sessions. MITI Global Clinician Ratings averaged 4.91 ± .15 on a scale of 1-5, well above the threshold for competency, and higher than scores typically recorded after a two-day training.
Conclusions: The two-stage interventionist training used in this study produced excellent results across the first 8 interventionists trained. Focusing first on fundamentals and later on specific intervention content may bestow an advantage for learning and implementing brief interventions based on a motivational interviewing approach.
Financial Support: NIDA CTN

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FREQUENCY OF AND RESPONSE TO WITNESSED OVERDOSES AMONG DRUG USERS.

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Aims: Witnessing a member of one's drug network overdose is common among users of heroin and cocaine. Witnesses of an overdose can respond in order to reduce the risk of fatality, and overdose prevention programs that train heroin users to act in a way to prevent fatality are effective. The present study examined participants characteristics associated with the count of overdoses ever witnessed and the association of actions taken at the last overdose witnessed with the number of overdoses ever witnessed.
Methods: Persons in New York City who had used heroin or cocaine in the prior two months completed a structured in-person interview (n=1,093). Modeling included multivariable negative binomial and multinomial regressions.
Results: Those persons who used heroin (IRR=2.0, 95% CI: 1.3, 3.2), have been homeless (IRR=1.9, 95% CI: 1.4, 2.6), inject multiple drugs together (IRR=1.6, 95% CI: 1.2, 2.1) and have overdosed (IRR=1.9, 95% CI: 1.6, 2.4) reported a greater count of witnessed overdoses. Persons who had witnessed more overdoses in their lifetime were less likely to report that the victim was taken to the hospital (OR=0.6, 95% CI: 0.4, 0.9) and more likely to report that the victim was injected with water, salt, speed, or bleach (OR=2.8, 95% CI: 1.6, 4.8) at the last overdose witnessed compared to persons who had witnessed fewer overdoses.
Conclusions: Individuals who are at greater risk of overdose witness more overdoses, suggesting that overdose risk clusters within drug networks. Individuals who have witnessed more overdoses were less likely to take effective action at the last overdose witnessed. The present findings suggest that individuals who have elevated overdose risk themselves are an appropriate target of witness-based overdose prevention interventions. Such interventions are needed to improve use of appropriate responses to overdose for individuals who have witnessed many overdoses.
Financial Support: NIH grants R01DA006534, R01DA012801S1, and R01DA017642 and VA grant CDA-09-204

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THREE-MONTH EFFICACY OF A BRIEF INTERVENTION FOR REDUCING MARIJUANA USE AND CONSEQUENCES AMONG ADOLESCENTS PRESENTING TO INDIGENT PRIMARY CARE CLINICS.

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Aims: This paper describes the efficacy of a brief intervention addressing marijuana use among adolescents presenting to indigent primary care clinics.
Methods: Patients aged 12 to18 years were approached at inner-city primary care clinics in Michigan and asked to complete a self-administered computerized survey. After completion of the baseline survey, participants who reported past-year marijuana use were enrolled in a randomized controlled trial (Project CHILL) (n=328). The participants were then randomized to a 30 minute brief intervention delivered by a computer or therapist, or to a control group. 85% (n=279) completed a follow-up assessment at 3 months to assess marijuana use and consequences. A negative binomial regression approach, applying generalized estimating equations, was used to examine intervention effects on 3 month marijuana use and consequences.
Results: At 3 months, all three groups showed reductions in past 3 month marijuana use (therapist=2.6%; computer=7%; control=2.8%). Compared with the control group, participants in the computer intervention had a statistically significant greater reduction in the number of marijuana consequences (coefficient=-0.43; p=0.01); reduction among participants in the therapist group was not statistically robust (coefficient=-0.14; p=0.4).
Conclusions: Findings support the initial efficacy of a computer-delivered brief intervention in reducing marijuana consequences. Future research is needed to examine longer-term outcomes and to assess the effectiveness of the computerized intervention in other settings.
Financial Support: NIDA R01 020075

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USING FACEBOOK TO MAXIMIZE FOLLOW-UP RESPONSE RATES IN A LONGITUDINAL STUDY OF ADULTS WHO USE METHAMPHETAMINE.

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Aims: In longitudinal research reducing non-response bias and increasing validity can be a challenging task especially when working with an illicit drug using population. This study examines the process and effects of using facebook (FB) to locate and re-contact study participants targeted for follow up in a longitudinal study of adult methamphetamine (meth) users.
Methods: Data are from an intensive natural history study of adults in Los Angeles County who used meth regularly; half received substance abuse treatment in the mid-1990s (n=350), were interviewed in 1999-2001 and again about two years later; and half had not received treatment (n=299) and were interviewed once in 2001-04. The current study, beginning in 2009, is a follow-up of both samples (N=649) to examine the life course and long-term outcomes of meth users. Our paper describes the FB process including IRB regulatory issues specific to privacy and confidentiality, the study FB page, contact procedures, and the effectiveness of using FB compared to mailing and phone calls. Cross tabulations (chi square) and means (t-test or ANOVA) are used to describe the demographic and substance use history of participants contacted through FB and compare to those without FB contact.
Results: A total of 33 of the 561 surviving non-incarcerated participants who agreed to be contacted for follow up studies were contacted via FB of which eight responded back. Prior to FB contact an average of six phone calls and nine unsuccessful mailings were attempted to contact each of the 33. Those contacted through FB were younger, had a higher level of education, and fewer were incarcerated at the first interview. On average, those contacted through FB were about 2.5 years younger when they first started using meth than those not contacted through FB ($p=.034$).
Conclusions: Although participants contacted through FB are likely to differ demographically from those contacted by phone or mail, FB provides an efficient and effective alternative to conventional methods of correspondence for contacting hard to reach participants.
Financial Support: NIDA DA025113

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DESIGNER DRUGS, SYNTHETIC CANNABINOIDS AND THEIR RELATED PRODUCTS SPICE, K2 AND MANY OTHERS.

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Aims: The Drug Enforcement Administration (DEA) monitors and collects information regarding the emergence of new substances to the designer drug markets and responds to these issues in accordance with the threat to public health and safety. The abuse of synthetic cannabinoids and products laced with these substances are a recent law enforcement and public health phenomenon.
Methods: DEA works closely with other agencies to collect scientific information and evaluate substances for a possible scheduling action. Acute and long term health effects and safety issues are evaluated in response to the abuse of these substances. Additionally, data from scientists, law enforcement and public health are critical to the evaluation process.
Results: As an indicator of availability and abuse, synthetic cannabinoids are increasingly being encountered by law enforcement and public health officials. These substances and related products are often marketed as legal alternatives to cannabis and are widely available from internet websites, head shops, and convenience stores. Health warnings have been issued by numerous state public health departments and poison control centers describing the adverse health effects associated with synthetic cannabinoids and their related products. Case reports describe psychotic episodes, withdrawal, and dependence associated with these synthetic cannabinoids, similar to syndromes observed with cannabis abuse.
Conclusions: Very little information is known of the acute and chronic effects of synthetic cannabinoids in humans therefore, further pharmacological evaluation is needed. This information will play a crucial role in evaluating these new substances for a possible scheduling action under the Controlled Substances Act (CSA). DEA will continue to collect scientific information and work closely with other agencies to assess risks to the public posed by synthetic cannabinoids and pursue controls as appropriate.
Financial Support: Drug Enforcement Administration

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ADENYLYL CYCLASES TYPES 1 AND 8 ALTER BEHAVIORAL RESPONSES TO TOLUENE.

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Aims: Although the abused inhalant toluene is known to have potent neuronal effects, only recently has progress been made in understanding the molecular pathways that mediate toluene's action in the brain. In research with other drugs of abuse, mice lacking the calcium-stimulated adenylyl cyclases (ACs), AC1 and AC8 (DKO), show increased sedation durations and impaired phosphorylation by protein kinase A (PKA) following acute ethanol treatment. In the present investigation, both DKO and wild type (WT) mice were studied for their acute sensitivity to toluene-induced changes in locomotor activity.
Methods: Mice were exposed to toluene (0, 500, 1000, 2000, 6000, 8000 ppm) for 30 min in static exposure chambers equipped with activity monitors. Following toluene exposure, mice were monitored for locomotor activity during a 30 min recovery period during which they were exposed to air only.
Results: Concentrations of toluene at 1000 and 2000 ppm increased ambulatory distance in WT mice (with attenuated responses in DKO mice) while concentrations of ≥6000 ppm induced largely hypoactive effects in WT and DKO mice as compared to air controls. Within the recovery period, significant increases in locomotor activity were observed at 2000 ppm as compared to air controls in WT mice, although toluene-exposed DKO mice demonstrated a significantly reduced response at this dose. Sedative effects of toluene resulting from high doses (6000-8000 ppm) were equivalent in WT and DKO mice, both during exposure and recovery.
Conclusions: Together, these data suggest that the calcium-stimulated cyclases, AC1 and AC8, mediate the molecular pathways that sub-serve toluene-induced hyperactivity both during and following toluene inhalation.
Financial Support: Supported in part by funding from WSU Department of Neurosurgery (Conti) and WSU Bridge Funding (Bowen).

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EIGHT WEEKS OF CITICOLINE TREATMENT DOES NOT AFFECT SLEEP OR COGNITIVE FUNCTION IN NON-ABSTINENT COCAINE-DEPENDENT ADULTS.

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Aims: Citicoline is involved in the biosynthesis of structural phosopholipids of cell membranes. Several aspects of treatment with citicoline (improved memory in dementia, and reduced brain damage after traumatic brain injury or stroke) suggest that it may be a candidate adjunct treatment for cocaine dependence. In cocaine-dependent individuals, abrupt withdrawal is associated with disturbed sleep, which may contribute to deficits in cognition and increased relapse rates. This double-blind, placebo-controlled trial assessed the effects of citicoline on sleep and cognitive function in cocaine-dependent participants.
Methods: Twelve cocaine-dependent adult (age 36.3±1.4 years) men (n=7) and women (n=5) completed 2 week baseline, 8 week treatment [placebo n=4; citicoline n=8 (500 mg, b.i.d.; Grupo-Ferrer International, Barcelona, Spain)], and 2 week follow up phases. Participants kept a daily diary of subjective sleep measures, wore a wrist actigraphy device (ActiWatch-Score, Mini-Mitter/Respironic) from which sleep parameters were calculated, and completed cognitive testing during each phase. For each participant, all data were averaged for each phase; within-subject ANOVAs were run on averaged data.
Results: Citicoline had no effect on the following variables (all analyses resulted in p values of 0.29 – 0.92): actigraphy data (sleep efficiency index, sleep latency, total sleep time, number of waking episodes, time awake per episode, mobile time, number of sleep episodes, time asleep per episode, immobile time, average daily activity); subjective measures (sleep quality, feel rested, number of waking episodes, number of hours slept); cognitive function (Trail Making, Digit Symbol Substitution, Block Design, and Wisconsin Card Sorting Tasks).
Conclusions: There were no significant changes in cocaine use patterns during the treatment phase, so these data suggest that in non-abstinent, cocaine-dependent participants, 8 weeks of citicoline administration does not interfere with sleep/wake cycles or cognitive function.
Financial Support: NIDA grants DA011098, T32 DA15036, and K05DA00343.

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USE OF RX STIMULANTS FOR A REASON OTHER THAN PRESCRIBED: HOW OPERATIONALIZATION AFFECTS PREVALENCE RATES FOR NON-MEDICAL USE IN ADOLESCENTS.

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Aims: Non-medical use (NMU) of prescription drugs is use without a prescription or use in a manner other than prescribed. Use in a manner other than prescribed is not always assessed. In diagnostic interviews (SAM, DIS), use in a manner other than prescribed is operationalized as taking the drug more than prescribed, longer or more often than prescribed, or for a reason other than prescribed. The effect of "use for a reason other than prescribed" on prevalence estimates for NMU of Rx stimulants is examined.
Methods: Data come from the National Monitoring of Adolescent Prescription Stimulants Study (N-MAPSS): 2,798 10-18 year olds from 10 U.S. metropolitan areas were recruited at entertainment venues and completed an anonymous paper and pencil survey in 2009. Youth who had ever taken Rx stimulants (n=412) were asked if it was prescribed for them and if they ever used an Rx stimulant: A) to get high; B) out of curiosity; C) because pressured to; D) to stay awake; E) to lose weight; F) to study; G) to relax; H) just because; I) instructed by doctor or parent; J) safer than street drugs; K) to be cool. Three alternative methods of coding lifetime NMU of Rx stimulants were compared.
Results: The reasons for use endorsed by over 50% of un-prescribed users (n=171) were A (61%), B (70%), D (53%) and H (53%). The reasons for use endorsed by prescribed users (n=218) were F (49%) and I (73%). A small group (n=23) who reported use both with and without a prescription are included in the 47% rate for lifetime NMU based only on un-prescribed use. Adding prescribed users who endorsed reasons A, B and H increased the rate of NMU to 55%; any reason other than F or I increased lifetime NMU prevalence to 68%.
Conclusions: Assessment of NMU among young Rx stimulant users can yield disparate prevalence estimates. We found that young prescribed users will endorse reasons for use that are not medically indicated.
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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DELAY DISCOUNTING PREDICTS SMOKE STATUS DURING PREGNANCY.

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Aims: Smoking during pregnancy is a leading preventable cause of poor pregnancy outcomes. Only approximately 20% of smokers quit upon learning of a pregnancy while the remaining 80% smoke throughout their pregnancy. One factor that may contribute to continued smoking during pregnancy is delay discounting (DD). DD describes the rate at which rewards lose value as the delay to their receipt increases. For a woman to quit smoking during pregnancy she has to forgo the immediate reinforcement that cigarette smoking provides in order to obtain delayed reinforcement associated with a healthy pregnancy and infant. In the present study we aimed to assess whether DD predicted quitting or continuing to smoke during pregnancy after controlling for pre-pregnancy smoking rate and education, the two largest predictors of continued smoking during pregnancy reported previously (Higgins et al. 2009).
Methods: Subjects were 209 pregnant women who reported being smokers at the time of conception; 136 were still smoking upon entering prenatal care while 73 quit shortly after learning of the pregnancy. To assess DD, participants made choices for two different hypothetical monetary options, a fixed delayed $1000, or a smaller amount available immediately. Smaller reward values were presented across trials according to an algorithm until an indifference point was found. An indifference point (IP) was determined for 7 delays (1 day-25 years). Individual rates of DD were determined by obtaining a k-value rate parameter from a hyperbolic equation fit to the individual IPs for each subject (Mazur, 1987).
Results: DD was a significant predictor of continuing to smoke during pregnancy after controlling for pre-pregnancy smoking rate and education. For each unit increase in k there was an 18% increase in the likelihood of being a continued smoker (OR = .82, .70-.95, p = .01).
Conclusions: This DD rate difference may reflect a stable fundamental decision-making deficit among pregnant continued smokers, which has implications for a broad range of health behaviors affecting these women and their children.
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MONITORING PRESCRIPTION DRUG ABUSE THROUGH COMMUNITY PHARMACIES: A FEASIBILITY STUDY.

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Aims: Regular users of prescription psychotropics encompass more than patients who attend pain or specialty clinics, and they may be at increased risk for abuse of these drugs. The objective of this study was to establish the feasibility of conducting telephone interviews to characterize regular users identified through community pharmacies.
Methods: Phase 1. Prescription records from 8 pharmacies were summarized to provide the number of current regular users of opioids, sedatives, and stimulants, using predefined criteria. Phase 2. Pharmacists invited eligible regular users to call study personnel to undergo a telephone interview.
Results: Of invited regular users, approximately 14% of opioid, 7% of sedative and 0% of stimulant users called. The characteristics of the regular user groups compared to those who called were similar in terms of age, gender, and types of opioids and sedatives used. Interviews took 88 ± 23 minutes. Of the regular opioid users interviewed (n=23, mean age 53 ± 9.4 years, 61% female), 35% (n=8) scored 9 or higher on the Current Opioid Misuse Measure (COMM) indicating a high risk for abuse. The total daily dose of opioids did not differ between the low and high scoring COMM groups (990 vs 744 mg, morphine equivalents, ns). Most were using oxycodone (44%) or codeine (39%). Only 65% had tried non-opioid analgesics. Seventeen percent considered their current use of opioids a problem (20% vs 12%, low and high COMM groups, respectively, ns). Of the regular sedative users interviewed (n=24, mean age 54.5 ± 9.6, 50% female), most were using clonazepam (38%) or lorazepam (29%), and 38% were taking more than 1 type. They used regularly for 12 ± 8 years, with a current total daily dose of 36 ± 28 mg diazepam equivalents. Only 1 subject considered their sedative use a problem.
Conclusions: This small scale study suggests it is feasible target this population through community pharmacies, and the characteristics of these regular users warrants further research.
Financial Support: Health Canada

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LONG-TERM (13-YEAR) OUTCOMES OF TREATMENT OF METHAMPHETAMINE USE.

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Aims: This study examines methamphetamine (meth) use and predictors of relapse over a 13-year period following treatment in a sample of individuals treated for meth.
Methods: Data (n=166) are from a current follow-up study of individuals treated for meth abuse in Los Angeles County in the mid-1990s; intensive natural history interviews were conducted approximately 3, 6, and 13 years after treatment. Outcomes examined included time to relapse following treatment (Cox proportional hazards models) and any 5-or more year period of abstinence (logistic regression) during the long-term follow-up period, with selected predictors from demographic, early family and substance use history, and treatment-related domains.
Results: The analysis sample was 48% female, 46% non-Hispanic White, 28% Hispanic, 19% African American, and 7% other race/ethnicity. 14% have maintained continuous abstinence from meth use since the studied treatment episode. An additional 48% had periods of abstinence of at least 5 years duration during the 13-year follow-up period, but also had some periods of meth use. In the multivariate Cox model, significant ($p<.05$) predictors of longer time to relapse, controlling for the propensity to participate in post-treatment self-help were: greater percentage of months employed and lower meth use severity in the 2 years preceding the studied treatment episode, longer time in that treatment episode, and more months in additional treatment and/or self-help in the 2 years following the episode. Demographic, early family history, and substance abuse history were not predictive of long-term continuous meth abstinence. Differences in predictors of 5-year abstinence are also discussed.
Conclusions: While few in this sample maintained continuous long-term abstinence following the identified treatment episode, a total of 62% had periods of abstinence of at least 5 years. Continuing care (through self-help and/or additional treatment) in the first 2 years following treatment is strongly predictive of longer duration continuous post-treatment meth-abstinence, supporting a focus on assuring availability of such services.
Financial Support: NIDA DA025113

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TOBACCO USE AMONG AFRICAN-AMERICAN YOUTH BEING TREATED FOR BEHAVIORAL HEALTHCARE ISSUES.

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Aims: Approximately 24% of high and 8% of middle school students and use tobacco; rates among African-American (AA) youth tend to be lower (14% among high and 8% among middle-school students; CDC, 2010). Adolescents with behavioral healthcare problems (substance abuse and/or mental health) are particularly vulnerable to tobacco initiation and dependence, yet little is known about rates of tobacco use among AA youth in this group. The purpose of this study was to examine rates of smoking among AA youth being treated for mental health or substance abuse disorders at a public behavioral healthcare organization, and determine differences between tobacco users and non-users.
Methods: Retrospective chart reviews were conducted at one urban, public behavioral healthcare agency in Virginia for all youth aged 13-17 who were admitted for mental health and/or substance abuse treatment during FY 2009.
Results: 201 admissions were reviewed. Most (95%) of the sample was AA, and the average age of youth was 15 years. Nearly all (97%) were screened for tobacco use. Twenty-eight percent of youth reported using tobacco, higher than national rates, and nearly twice as high as high school students in Virginia (YTS, 2009). Tobacco users were more likely to be male than female (79% vs 21%). Compared to non-tobacco users, tobacco users tended to be older (16 years vs 15 years), were more likely to have a substance abuse diagnosis, (74% vs 26%), and were more likely to say they had ever used marijuana (75% vs 25%; all ps < .05). Only 4% were treated for tobacco use.
Conclusions: In this sample, rates of smoking among AA youth being treated for mental health and or substance abuse disorders were higher than in the general population. While tobacco cessation programs should be implemented for all adolescents receiving behavioral healthcare, a special focus should be placed on youth in this demographic as they may be at higher risk for tobacco-related morbidity and mortality.
Financial Support: Supported by Virginia Foundation for Healthy Youth Grant #8520666

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CIGARETTE SMOKING AS A TARGET FOR POTENTIATING OUTCOMES FOR METHAMPHETAMINE USE TREATMENT.

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Aims: Frequent co-administration of methamphetamine and nicotine represents a pharmacologically meaningful pattern: Adolescent exposure to nicotine presages subsequent MA use; nicotine priming reinstates MA-seeking behavior following MA withdrawal; the substances cross-potentiate behavioral and neurochemical responses, and nicotinic acetylcholine receptors are implicated in the neuroadaptations associated with stimulant abuse. Elucidating temporal links between nicotine use and MA treatment
response may highlight relevant pharmacological targets.
Methods: Forty-eight treatment-seeking MA-dependent cigarette-smoking participants were included in these post hoc analyses, selected from a larger 12-week randomized, placebo-controlled, double-blind study of bupropion (300mg/daily). Participants' (bupropion N=29; placebo N=19) MA use was assessed thrice weekly by urine samples and self-report cigarette smoking was assessed weekly. Hierarchical regressions were implemented to assess the longitudinal relationships between nicotine and MA use.
Results: Cigarette smoking and MA use was positively correlated among participants in both active and control conditions. When controlling for time, there was no evidence of longitudinal dependencies between cigarette smoking and MA use.
Conclusions: These analyses indicate that changes in cigarette use do not portend positive or negative MA-related outcomes. High levels of missingness, sample size, and nonlinearities observed in the data may have constrained the ability to detect meaningful longitudinal associations. The lack of initial findings for a temporal link between cigarette smoking and MA use suggest that targeting cigarette smoking as a component of MA dependence treatment is not likely to substantially improve clinical outcomes.
Financial Support: NIH 1 P50 DA18185 & 1 T32 DA026400

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MINDFULNESS TRAINING FOR SMOKING CESSATION: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL.

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Aims: Cigarette smoking is the leading cause of preventable morbidity and mortality in the US, and abstinence rates for current treatments remain modest. Stress and craving may be important in quitting, but few interventions have targeted these and related affective states. Data suggest that Mindfulness Training (MT) may be effective for the treatment of addictions by targeting stress and craving, but no randomized trials have examined it for smoking cessation.
Methods: 88 treatment-seeking, nicotine-dependent adults who were smoking an average of 20 cigarettes/day were randomly assigned to receive MT or the American Lung Association's Freedom From Smoking (FFS) treatment. Both treatments were delivered twice weekly over four weeks in a group format. The primary outcomes were carbon monoxide-confirmed 7-day point prevalence abstinence and number of cigarettes/day. Data were collected during treatment and at follow-up at week 17.
Results: 88% of individuals who received MT and 84% of individuals who received FFS completed treatment. Compared to those randomized to the FFS intervention, intent-to-treat analysis revealed that individuals who received MT had a greater reduction in cigarette use during treatment and maintained these gains to a greater extent during the follow-up period ($F=11.11$, $p = .001$). They also exhibited a greater point prevalence abstinence rate at the end of treatment (30% vs. 13%, $p = .078$) and the 17-week follow-up (24% vs. 5%, $p = .022$). Additionally, strong correlations were found between specific types of home practice and outcomes in the MT group, but none were found in the FFS group.
Conclusions: MT may confer benefits greater than those associated with current standard treatments for smoking cessation. These benefits may be specific to particular types of mindfulness practice.
Financial Support: This study was funded by the following grants: NIDA K12-DA00167, P50-DA09241, K05-DA00457, K05-DA00089, UL 1 DE019586-02, and the U.S. Veterans Affairs New England Mental Illness Research, Education, and Clinical Center (MIRECC).

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PROGRESSION OF POLYSUBSTANCE ABUSE AND DEPENDENCE SYMPTOMS IN A LONGITUDINAL CLINICAL SAMPLE.

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Aims: This longitudinal study examined several characteristics of the development of abuse and dependence symptoms among matched clinical treatment and community subjects using two waves of data collection. It was expected that clinical subjects would be distinguished by earlier symptoms from illicit drug use, higher lifetime maximum symptom counts, and earlier age of onset for symptoms of any drug, both legal and illicit.
Methods: The sample includes 279 young adults (9% female) admitted to a residential treatment center for antisocial drug dependence and 155 young community adults (15% female) originally matched on age, gender, ethnicity, and zip code. Retrospectively recalled onset and recency of reported symptoms at Wave 2 (6 to 10 years following Wave 1) were used to estimate annual symptom counts to generate individual drug symptoms trajectories.
Results: : Excluding the 22% of community subjects reporting no symptoms of drug abuse or dependence, community subjects were more likely to experience symptoms from alcohol only (25% vs. 3% clinical; $\chi^2 = 49.31$, $p < .001$), while clinical subjects were more likely to endorse symptoms from multiple substances. Clinical subjects were also more likely than community subjects to choose as their first drug either cannabis (27% vs. 17%; $\chi^2 = 4.13$, $p < .05$) or other illicit substances (5% vs. 0%; $\chi^2 = 4.50$, $p < .05$). Linear regression analysis of individual trajectory parameters found that, for both samples, earlier age at first symptom of any drug predicted lifetime maximum symptom count. Across all individuals, each year of delayed onset was associated with a 1.9 ($p < .001$) unit decrease in the peak drug symptom count—controlling for gender and Wave 2 reporting age.
Conclusions: Clinical polysubstance users are distinguished by earlier drug symptoms, particularly from illicit substances, as well as more symptoms at lifetime peak use.
Financial Support: Supported by funding from the National Institute of Drug Abuse to the Center for Antisocial Drug Dependence (DA011015, DA021913, DA012845), and NIAAA Training Grant (AA007464).

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PRELIMINARY FINDINGS FROM TWO STUDIES OF LONG-TERM RECOVERY MANAGEMENT FOR PERSONS WITH STIMULANT OR OPIATE DEPENDENCE.

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Aims: Study #1 determine feasibility of Long Term Recovery Management (LTRM); would pariticipants 1) attend the sessions and remain engaged with a recovery manager, 2) comply with research assessment procedures. Study #2 compares effectiveness of TAU & TAU + LTRM for treatment seeking adults with stimulant or opioid dependence.
Methods: Study #1 Enroll 10 cocaine dependent outpatient adults who use crack into LTRM. LTRM consists of extending treatment enrollment to 12 months, individual sessions to facilitate therapeutic alliance, CRA style groups, prize based contingency management for attendance, and an algorithm to adjust treatment intensity. Assessments at baseline, 3, 6, 9 & 12 months. Study #2 Randomize 203 adults with opiate or stimulant dependence to either TAU or TAU + LTRM. Assessments at baseline, 6 months and 12 months.
Results: Study #1: enrolled 10 adult crack users, mean age of 44, 80 % male, 90% African American. Participants attended 100% of individual sessions, 52% of group sessions; follow-up rates were 90%, 100%,90% & 60% @ 3, 6, 9, & 12 months respectively. Percent days of cocaine use reduced from 51 at baseline to 25, 24, 21,& 26 @ 3, 6, 9, & 12 months respectively. Study #2: 203 opiate or stimulant dependent adults enrolled in ongoing trial. Current follow-up rates of 85% & 97% at 6 & 12 months respectively. Participants are 67% male, average 34 years of age, 22% African American, 65% abuse stimulants, 63% opioids, & 69% alcohol.
Conclusions: Study #1: LTRM shows good feasibility. Study #2: Trial is ongoing feasibility conclusions of study #1 supported and treatment exposure and baseline severity data will be available for presentation.
Financial Support: Study #1 Maryhaven, Wright State University & NIDA #1K23DA021512(PI Brigham) Study #2 NIDA Grant #1K23DA021512(PI Brigham)&1RC1DA028467 (PI Carlson)

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HOW DOES EXPOSURE TO A 'BINGE' DOSE OF MDMA AFFECT BEHAVIOR OF RATS TRAINED IN A THREE-WAY DRUG DISCRIMINATION?

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Aims: Previous drug discrimination studies have shown that 3, 4-methylenedioxymethamphetamine (MDMA; 'Ecstasy') shares psychoactive effects with both stimulants and hallucinogenic compounds. Many of MDMA's distinctive effects and toxicity have been linked to its actions on serotonergic neurotransmission. One way to more selectively examine these serotonergic effects is to train rats to distinguish between dopaminergic stimulant effects and mood and perception-altering serotonergic effects using a three-way drug discrimination paradigm.
Methods: Male and female Sprague-Dawley rats (n=18) were trained to reliably differentiate between amphetamine (0.75mg/kg), MDMA (1.5mg/kg) and saline. The contributions of serotonin1A (5-HT1A) and 5-HT2A/C receptors to MDMA's interoceptive effects were evaluated both before and after the rats were exposed to an MDMA 'binge' (3 x 10mg/kg at two hourly intervals), to determine whether this reportedly neurotoxic dosing regimen would disrupt the interoceptive cues of MDMA.
Results: Blockade of 5-HT1A or 5-HT2A/C receptors, via administration of WAY 100,635 (1 mg/kg) or ritanserin (1.5 and 3 mg/kg) respectively, significantly and selectively disrupted MDMA-appropriate responding. Binge MDMA administration also selectively disrupted the MDMA training cue in the majority of rats during the subsequent two weeks. However once the discrimination had recovered, re-testing with the antagonists showed that the contributions of 5-HT1A and 5-HT2A/C receptors to the MDMA discriminative cues were not significantly different to what was measured prior to the 'binge'.
Conclusions: This study provides support for the importance of 5-HT1A and5-HT 2A/C mediated cues in the distinctive interoceptive effects of MDMA and suggest that these serotonergic discriminative stimulus effects are only temporarily disrupted following high-dose MDMA exposure.
Financial Support: This work was supported by a Clive and Vera Ramaciotti Establishment Gift; MDMA, WAY100,635 and ritanserin were generously provided by Prof. Susan Schenk.

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EVIDENCE-BASED MULTIMEDIA TOOLKITS IMPROVE COUNSELOR ADHERENCE IN GROUP COUNSELING WITH MINIMAL TRAINING: PRELIMINARY RESULTS.

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Aims: Numerous psychosocial interventions effectively improve client outcomes in clinical trials, but adapting evidence-based protocols into disseminable formats suitable for community treatment programs is challenging. As part of two NIH-funded clinical trials, we translated proven psychosocial treatments into multimedia curricula toolkits (TK) to help counselors deliver clinically useful group sessions that convey core elements of cognitive-behavioral relapse prevention (RP) and 12-Step facilitation (12SF); we tested the TKs' conceptual fidelity, utility, and attractiveness.
Methods: TK development was informed by consultation with content experts, counselors and clients, to develop simple, engaging presentations of core RP and 12SF concepts. Each TK session includes a brief introductory video, colorful posters and worksheets, recovery cards, and brief content outlines for counselors; materials link thematically, using repetition and modeling. In a pre-post design, we coded 4 treatment groups (client N = 293) run by 10 counselors: 2 standard groups and 2 groups on preselected RP topics, Coping with Craving (CC) and Drug Refusal (DR). Counselors attended a 3-hour training to familiarize them with the TKs; they received no direct training or supervision on these particular sessions. Observers attended and coded 4 additional post-training groups run by counselors using the TKs, including Toolkit groups for CC and DR.
Results: There was significant, large effect improvement in frequency and extensiveness in delivering CC (paired t = -5.17, p = 0.008, d = 1.68) and DR content (paired t = -3.21, p = 0.011, d = 1.74) with TKs; skillfulness of delivery did not significantly change.
Conclusions: Preliminary results show that multimedia toolkits may be a cost-effective, disseminable approach to improve group counseling in community treatment with minimal training.
Financial Support: NIDA R01 DA025034
NIAAA R01 AA017867

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IMPACT OF CIGARETTE USE ON TREATMENT OUTCOME IN BLUNT SMOKERS AND OTHER CANNABIS USERS IN A CANNABIS-DEPENDENT SAMPLE.

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Aims: Smoking tobacco along with marijuana has been associated with a greater number of cannabis dependence symptoms. The purpose of this study was to determine if individuals with cannabis dependence (CD) responded differently to treatment based on additional use of nicotine through cigarette or blunt use.
Methods: The sample (n=156) was 82% male; 49% Caucasian, 21% African American, 24% Hispanic and 6% other (age= 38). All participants met criteria for current CD based on the SCID for DSM-IV and were participating in a 12 week double blind, placebo controlled trial of Dronabinol for the treatment of CD. Marijuana groups (MJ) were defined as joint (36%), blunt (35%), or bowl/bong users (29%). Chronic cigarette smokers (CS) were defined as smoking an average of >/= 5 cigarettes/day;17% of the sample was CS. Treatment outcomes were defined as 1) weeks in treatment, 2) two consecutive weeks of abstinence and 3) a 50% reduction in weekly marijuana use at the end of the study.
Results: There were no differences in the rates of CS between the MJ groups. There was a significant racial difference in the MJ groups; 87% of the bowl users were Caucasian and 76% of the blunt users were African American or Hispanic (p=.00). Joint users were older than blunt users (43 vs. 32, p=.00). Logistic regression (including age, race, mode of MJ use, CS and study arm) revealed that blunt users were less likely to achieve two weeks of abstinence (25%) compared to joint users (35%) and bowl/bong users (40%) (p=.03). There was no difference in weeks retained in treatment or reduction in weekly marijuana use. The relatively low number of CS may be responsible for there being no observable effect. If you re-defined cigarette users as smoking any cigarettes and compared them to non-users, fewer users experienced 2 weeks of abstinence (24% vs. 41%, p=.03).
Conclusions: Further, since there may be some admixed tobacco with blunt smoking, it cannot be ruled out that blunt smokers may have a differing response to treatment due to their chronic use of cannabis plus nicotine.
Financial Support: NIDA Grant# P50DA09236

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IMPROVING ATTENDANCE TO SPECIALIZED PSYCHIATRIC SERVICES OFFERED IN A METHADONE TREATMENT PROGRAM.

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Aims: Services research on strategies to improve the care of drug-dependent patients with co-occurring psychiatric disorder is a high priority for treatment providers and health care policymakers. One promising approach involves the co-location and integration of psychiatric services in substance abuse treatment programs. Unfortunately, poor adherence to routine psychiatric services can limit the benefits of providing psychiatric care in substance abuse treatment settings. The present study reports on the efficacy of a contingency management intervention to improve utilization of psychiatric services offered in a methadone treatment program.
Methods: Subjects (n=44) in this ongoing randomized and controlled trial are opioid-dependent patients with comorbid psychiatric disorder that are randomly assigned to one of two psychiatric service delivery conditions: 1) on-site integrated psychiatric care with a voucher-based attendance reinforcement intervention (PCV); 2) on-site integrated psychiatric care without the attendance reinforcement intervention (PC). The same schedule and scope of psychiatric services were available to subjects in both conditions. Subjects were followed for three months post-randomization.
Results: The PCV (n=24) condition was associated with nearly twice the rate of attendance compared to the control condition (83% vs 42%; $p < .001$). PCV subjects also attended a higher percentage of weekly individual (PCV: 84% vs PC: 40%; $p < .001$) and group (PCV: 72% vs PC: 9%; $p < .001$) therapy sessions; interestingly, adherence rates to the sessions scheduled with a psychiatrist were both good and similar across conditions (90% vs 83%, ns).
Conclusions: The use of a relatively simple voucher-based reinforcement intervention targeting attendance to psychiatric treatment services significantly improved the overall adherence rate. The results should be viewed with caution because the sample size is only half the total number of subjects (N=80) that will be enrolled. It is unclear how much the improved attendance to individual and group therapies will affect treatment outcomes.
Financial Support: NIH-R01DA 016375
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RELATIONSHIPS BETWEEN INFECTION-RELATED KNOWLEDGE, OPINIONS, EXPERTISE, AND TRAINING AMONG CLINICIANS IN ADDICTION TREATMENT.

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Aims: In HIV care, evidence exists of relationships between clinical outcome and provider experience, knowledge, and expertise. However, relationships between clinician characteristics and availability of infection-related services have not been reported. We investigated these relationships among clinical staff and associations with availability of HIV counseling and testing services among addiction treatment programs.
Methods: In a cross-sectional, descriptive, multisite structured survey study, we analyzed responses from 269 addiction program administrators and 1716 clinicians concerning clinicians' infection-related opinions, knowledge, expertise, and training. Opinions were assessed using 5-point Likert scale, while the knowledge component contained 20 closed-end questions.
Results: Among 1350 non-medical clinicians, mean percent correct responses to knowledge questions was 53%. For 366 medical clinicians, mean percent correct responses to knowledge questions was 62%. Comfort discussing intimate sexual relationships with women having sex with women was endorsed by 79% of non-medical staff compared to 71% of medical staff, while 95% of non-medical staff viewed substance abuse prevention as important compared to 97% of medical staff. Mean percent correct responses was significantly associated with expertise and opinions of clinicians, and HIV testing, but not counseling availability. HIV counseling and testing was associated with ongoing staff training and experience, and the program administrators' opinion regarding necessity of full abstinence to successful HIV-related interventions.
Conclusions: This study provided empirical support for relationships between clinician knowledge and opinions, and relationships between availability of infection-related services and staff training, experience, and administrator opinions in addiction treatment programs.
Financial Support: National Institute on Drug Abuse (NIDA) as part of a cooperative agreement with the NIDA Clinical Trials Network (2 U10 DA13046)

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ONSET OF ABSTINENCE IN ADOLESCENTS TREATED FOR MARIJUANA AND ALCOHOL USE DISORDERS.

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Aims: To investigate time to onset of abstinence to identify treatment response in a sample of adolescent substance abusers participating in two independent behavioral treatment trials.
Methods: 175 Adolescents (47% African American) received 14 weeks of MET/CBT (n=67) or MET/CBT plus CM (n=108), which included contingent incentives for abstinence plus parent involvement. Teens in the Marijuana Trial reported marijuana use in the past 30 days or provided a THC-positive urine test, plus met DSM criteria for marijuana abuse or dependence. Teens in the Alcohol Trial reported alcohol use in the past 30 days, and either met DSM criteria for alcohol abuse or dependence or had had one binge episode (≥5 drinks in one day) in the past 90 days. Alcohol-dependent youth were excluded from the Marijuana Trial and were assigned to the Alcohol Trial. Youth eligible for both trials were assigned to the Alcohol Trial. Onset of abstinence from alcohol and marijuana was evaluated in all adolescents using discrete-time survival analyses and subsequent analyses were conducted by treatment and trial.
Results: No significant changes in abstinence occurred beyond the 6th week of treatment in adolescents being treated in either trial, with 46.3% of adolescents achieving abstinence by week 6. More youth in the Alcohol Trial became abstinent by week 6 (66.7%) than in the Marijuana Trial (35%). Abstinence rates by week 6 in the Marijuana Trial were 42.0% with CM and 27.5% with MET/CBT; 6 week abstinence rates in the Alcohol Trial did not differ by treatment.
Conclusions: Findings suggest that youth who are not responding to treatment by week 6 are unlikely to respond if they remain in their assigned treatment. A sequential multiple assignment randomized trial could be conducted to compare first line treatments (MET/CBT vs. CM), and to compare adaptive treatments for youth who are not abstinent by week 6.
Financial Support: NIDA DA015186, NIAAA AA016917, Arkansas Tobacco Settlement Proceeds

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RELIABILITY OF THE SEXUAL DISCOUNTING TASK: HIV RISK BEHAVIOR AND THE DISCOUNTING OF DELAYED SEXUAL REWARDS IN COCAINE DEPENDENCE.

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Aims: Cocaine dependence is associated with high rates of sexual HIV risk behavior, but little is known about the behavioral mechanisms contributing to this risk. One possible mechanism is delay discounting (devaluation of future rewards). Delay-discounting procedures assess preference between smaller immediate and a larger delayed rewards, with preference for immediate rewards being defined as greater delay discounting or impulsivity. Cocaine-dependence is associated with greater discounting for money rewards. To examine the contribution of delay discounting to sexual HIV risk behavior, the Sexual Discounting Task (SDT) assesses preference for unprotected sex now vs. delayed sex with a condom. A prior study in cocaine-dependent individuals showed that the SDT produces systematic data similar to the discounting of other rewards, suggesting delay discounting is relevant to understanding sexual risk behavior. The aim of the present study was to assess the test-retest reliability of the SDT in cocaine dependence.
Methods: Cocaine-dependent individuals (n=19) completed 2 sessions about 7 days apart in this ongoing study. Among stock photos of people whom participants were willing to have sex with, participants identified 4 individuals: most and least likely to have a sexually transmitted disease, most and least want to have sex with. For each condition, participants completed visual analog scales (VAS) assessing the likelihood of waiting for delayed sex with a condom vs. having unprotected sex now. The delay to protected sex increased across VAS up to 3 months. Area under the curve (AUC) was used to index discounting. Pearson correlations compared discounting between weeks 1 and 2 for each condition.
Results: Pearson correlations between sexual discounting at week 1 and 2 were positive and significant ($p < .05$) in three conditions, with a trend ($p=.11$) in the fourth condition.
Conclusions: The SDT is a reliable measure of hypothetical HIV sexual risk behavior in cocaine dependence, which supports its further examination in clinical research.
Financial Support: NIDA R21 DA026967

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COMPUTER-ASSISTED DELIVERY OF BEHAVIORAL TREATMENT FOR CANNABIS USE DISORDERS: PRELIMINARY RESULTS FROM A CONTROLLED TRIAL AND IMPLICATIONS FOR DISSEMINATION.

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Aims: The most potent outpatient intervention for cannabis use disorders is a combination of motivational enhancement therapy (MET), cognitive-behavioral therapy (CBT), and contingency-management (CM). To enhance potential dissemination, we have developed a computer-assisted version of this treatment. An ongoing randomized trial seeks to replicate findings from a prior uncontrolled study that demonstrated comparable efficacy for therapist- and computer-delivered MET/CBT/CM.
Methods: To date, 48 adults (M=34.8 yrs; 44% female, 56% African American) have been enrolled and assigned to one of three 12-week treatment conditions: computer-assisted MET/CBT/CM, therapist-delivered MET/CBT/CM or MET only. All treatments include twice-weekly urinalysis monitoring. MET/CBT/CM involves 9 counseling sessions with either a therapist or computer, and an abstinence-based reinforcement program. MET involves 2 therapist sessions and a participation-based reinforcement program.
Results: Preliminary findings (n=39) suggest that both MET/CBT/CM conditions engender more weeks of documented cannabis abstinence than MET alone, with no significant difference between therapist- and computer-delivered MET/CBT/CM (therapist: M=4.5; computer: M=3.4; MET=1.4). Retention rates between the two MET/CBT/CM conditions also do not differ significantly. Updated efficacy data along with preliminary post-treatment data, cost-effectiveness indicators, and findings related to ethnicity and gender will be provided for an expected sample size of 105.
Conclusions: If these preliminary findings are confirmed, they will replicate our and others' prior studies illustrating that computerized delivery of MET/CBT/CM is an efficacious alternative for various types of substance abuse problems. Implications of these findings for overall effectiveness and dissemination of behavioral interventions will be discussed.
Financial Support: NIDA: DA023526; Arkansas Biosciences Institute: Research Component of the Tobacco Settlement Proceeds Act

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BELIEFS SIGNIFICANTLY ASSOCIATED WITH THE CONSUMPTION OF ALCOHOL IN SCHOOL STUDENTS IN SPAIN.

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Aims: To determine the beliefs significantly associated with the consumption of alcohol in school students in Spain.
Methods: Sample: 991 students, 46,5% (n = 461) male, mean age 15,28 (SD=3.33). 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; administered in 21 schools in the Valencia City. It was applied logistical regressions, using as covariable the age, and three dependent variables: only have proved it, occasional consumption, and daily consumption.
Results: Among scholars that only have proved the alcohol, the associated beliefs are: "many times you do not know with what it's made" (OR=1,57), and "it can cause you mental illness" (OR=1,35). Among scholars that consume occasionally, the beliefs are: "requires a strong economic cost" (OR=1,43), "if you control nothing happens" (OR= 2,74), "it does not create problems" (OR=2,81); "is good for something" (OR=2,60); and to not answer "it harms people of surroundings" (OR=1,66); "many times you do not know with what it's made" (OR=1,47), and "it can cause you mental illness" (OR=1,81). And among those who consume daily, the beliefs are: "it doesn't cause problems" (OR=27,55), and to not answer "it causes many accidents" (OR=4,50).
Conclusions: Among scholars that consume alcohol occasionally or daily there are more beliefs that deny negative consequences of alcohol consumption. To believe that many times is not possible to know with what is made the alcohol beverage, and that it can cause mental illness the consumption of alcohol, are beliefs that have potential for preventing the consumption of alcohol after testing it once.
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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AUSTRALIA DRUG MARKET IN 2010.

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Aims: Australia's illicit drug markets constantly evolving. Recent years have seen a reduction in heroin supply and concomitant changes in the use of other drugs. This paper reports on 2010 trends in drug use in Australia, with particular reference to a new class of emerging analogue drugs.
Methods: The Ecstasy and Related Drugs Reporting System (EDRS) monitors the price, purity and availability of a range of substances including MDMA, methamphetamine, cocaine, GHB and ketamine. It also examines trends in the use and harms of these drugs. The data collection includes: a) surveys with regular ecstasy users (REU); b) surveys with key experts who have contact with regular ecstasy users through the nature of their work; and c) the analysis of existing data sources that contain information on ecstasy and other drugs.
Results: In 2010 693 participants who were regular ecstasy users completed a self-report survey about their patterns of drug use and associated harms. Self-reported use of MDMA has declined. National and global indicators of precursor and stockpile seizures also suggest a decrease in availability and purity of MDMA in Australia. A concomitant rise in use of mephedrone was noted. Sixteen percent of participants reported consuming mephedrone in the preceding six months prior to interview; with diverse prevalence by geographic region.
Conclusions: The Australian drug market is dynamic. We are now experiencing a decrease in the use of MDMA, stabilisation of other drugs and emerging use of analogue drugs, particularly mephedrone. The patterns of use differ by jurisdiction.
Financial Support: Australian Department of Health and Ageing

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UNODC TREATNET II: WORKING TOWARDS EVIDENCE-BASED DRUG DEPENDENCE TREATMENT AND CARE. CAPACITY BUILDING CASCADE: PRE-POST ASSESSMENT AND TRAINING SATISFACTION DATA.

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Aims: The United Nations Office on Drugs and Crime (UNODC) initiated Treatnet II in 2008. The project aims at improving the technical capacity for the provision of evidence-based drug dependence treatment and care services, including their capacity to support HIV and AIDS prevention. Treatnet advocates for the concept of drug dependence as a multifactorial disease that should be treated with the same standard like any other health disorder.
Methods: The Treatnet II strategy includes three lines of action: Advocacy, Capacity Building and the development and strengthening of drug treatment services. Treatnet is currently active in more than 25 low-and middle income countries in Africa, Central Asia, Latin America and South East Asia. 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 (http://www.unodc.org/ddt-training/treatment), so that these can train staff in their countries and hence contribute to the development of a well qualified workforce delivering evidence-based drug treatment and care.
Results: The poster will present data from the Capacity Building Component, including the number of practioners trained, pre- and post-assessment as well as training satisfaction data.
Conclusions: The cascaded Train the Trainers approach guarantees sustainability of knowledge and skills transfer while reaching a high number of professionals.
Financial Support: UNODC

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PUBLIC HEALTH IMPACT OF INJECTING PRESCRIPTION OPIOIDS.

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Aims: Many abuse deterrent formulations (ADFs) of prescription (Rx) opioids are designed to inhibit abuse by unintended routes of administration (ROA) such as injecting, but these formulations are not necessarily expected to reduce abuse by swallowing. If an ADF does reduce successful tampering and abuse by unintended ROAs, what public health impact might be expected? This presentation focuses on functional problems reported by Rx opioid abusers who inject.
Methods: This study utilized the ASI-MV® Connect, a NAVIPPRO™ data stream, which collects product-specific abuse of opioids in the past 30 days, including ROA, in addition to data on problems associated with abuse (medical, employment, alcohol/drug use, legal, family/social, and psychiatric problems) from adult clients entering substance abuse treatment.
Results: Of 29,532 clients who abused an Rx opioid in the past 30 days, 66.3% reported no opioid injection, 4% reported injecting Rx opioids only (no heroin), and 29.7% reported injecting Rx opioids and heroin. Compared with non-injectors, injectors of Rx opioids only (no heroin) were significantly more likely to have one or more visits to the ER ($p<0.001$), were significantly more likely to report liver disease (including hepatitis A, B and C; $p<0.001$), and significantly more likely to report a pain problem ($p<0.001$). A trend was observed with regard to Rx opioid injectors reporting HIV/AIDS ($p=0.051$). Those Rx opioid abusers who reported injecting an Rx opioid and heroin were significantly more likely than non-injectors to report liver disease and HIV/AIDS ($p<0.001$ for both), but no more likely to report ER visits or a pain problem than non-injectors.
Conclusions: Preliminary data suggest some similarities between injectors of Rx opioids and pain patients (more ER visits and pain complaints) than those who inject Rx opioids but also inject heroin. Injectors of Rx opioids and heroin may be more like a non-pain patient abusing population. Such findings may go some distance toward an understanding of the possible public health impact of ADFs, especially as more ADFs enter the marketplace.
Financial Support: Inflexxion, Inc.

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SECONDARY DATA ANALYSIS USING ITEM RESPONSE THEORY TO IMPROVE MEASUREMENT OF RECOVERY.

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Aims: Research on the measurement of recovery from drug addiction is still lagging, despite the fact that recovery has important implications for addiction treatment. While traditional psychometric methods have served addiction researchers well in the past, a new generation of behavioral health measures based on the psychometric foundations of Item Response Theory (IRT) is being developed, but the activities are largely located outside of addiction research. The aim of this project is to apply IRT in secondary data analysis to screen and identify items that can enhance the measurement of recovery.
Methods: We conduct an analysis of data collected under the Drug Abuse Treatment Outcome Studies (DATOS). DATOS data sets contain a number of measures that are pertinent to recovery, e.g., substance use, employment/support, health, anxiety, depression, behavioral problems, psychological distress, motivation, etc.
Results: As a case-in-point, DATOS contains 20 items measuring the clients' motivation and readiness for treatment. IRT analysis indicates that some of the items may be of poor measurement quality. Dropping the items can potentially lead to a more refined set of items without noticeable loss of measurement precision. The IRT equivalent of the scale reliability coefficient of the unreduced scale is equal to .73, and for the reduced scale, .72.
Under the Psychological Distress domain, DATOS contains a set of 14 items that measure clients' internalizing symptoms. These items illustrate the applicability of the IRT-based differential item functioning detection procedure. Most notably, the item "crying easily" shows as a much less severe symptom for the female population than for males (chi-square = 135.3, df=5). The IRT model can tease apart the observed group difference into measurement non-equivalence and true difference.
Conclusions: IRT methods can help identify the domains of recovery, refine candidate items, check the dimensionality of the domains, and anticipate psychometric challenges that might arise in the future.
Financial Support: This research is supported by grants from NIDA (R01DA030466 and K05DA017648).

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DEVELOPING A COMPUTERIZED SEXUAL RISK ASSESSMENT AND FEEDBACK TOOL FOR USE IN SUBSTANCE ABUSE TREATMENT.

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Aims: The aim of the Being Safe in Treatment (BEST) project is the development of a sexual risk assessment and feedback tool to be used in substance abuse treatment programs. An audio computer-assisted self-interview HIV risk assessment previously used in a multi-site, RCT was modified for use as a brief assessment. A feedback report is generated that identifies a client's risk behaviors and how they compare to normative groups. Suggestions for reducing risk behaviors are provided. The BEST feedback report was modified in response to feedback provided in focus groups conducted with clients and counseling staff in a residential treatment center.
Methods: The BEST was subsequently administered to 61 men and 48 women in outpatient treatment in a pilot study with the aim of determining if receiving a BEST feedback report was associated with: 1) increased client-counselor discussion of sexual issues; 2) changes in variables associated with sexual risk behavior. The pilot study was not powered to detect differences, but instead had the goal of estimating effects as measured by odds ratios that would inform sample size needed for a future RCT. Participants were randomly assigned to receive (RR) or not receive (NR) a BEST feedback report in a 2:1 ratio. Those receiving a feedback report had the option of providing a copy of the report to their counselor (CR). To date 51 participants completed a follow up BEST assessment at 3 months.
Results: More CR clients (n=8, 53.3%)reported discussing sexual issues in counseling sessions in the 90 days prior to follow up than non-CR clients (n=11, 30.6%, OR=2.5). Fewer NR clients (n=2, 13.3%) reported using condoms during their most recent sexual event prior to the 90 day follow up than RR clients (n=16, 44.4%, OR=3.4). Fewer NR clients (n=4, 26.7%) possessed condoms at follow up than RR clients (n=20, 55.6%, OR=3.4).
Conclusions: The BEST assessment and feedback report shows promise of increasing client-counselor discussion of sexual issues, and condom use and possession.
Financial Support: NIDA grant R21DA022940 (D. Calsyn, PI).

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MULTI-LEVEL PREDICTORS OF RELATIONSHIP POWER AMONG DRUG-INVOLVED WOMEN.

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Aims: Gendered relationship power is linked to women's ability to reduce sexual risk behaviors which can lead to the transmission of HIV/AIDS. Drug-involved women have rarely been the focus of research on relationship power; however the intersection of gender, poverty, cumulative stress, and sexuality may uniquely impact this group. The current study examines empirical and theoretically derived multi-level predictors of relationship power among treatment-seeking, drug-involved women participating in a multi-site NIDA Clinical Trials Network HIV prevention intervention study.
Methods: Repeated measures data from 515 women was used to test eight a priori selected baseline predictors of relationship power (age, race/ethnicity, education, substance use, economic dependence, partner abuse, sexual concurrency, sex role identity) using mixed effects modeling. Power was measured using the Sexual Relationship Power Scale (Pulerwitz et al., 2000) comprised of two subscales: relationship control (i.e., personal empowerment) and decision-making dominance.
Results: Women with an abusive partner were more likely to report lower relationship control scores, however the impact of partner abuse decreased over time ($F=5.9$, $p<.01$); women with an abusive partner also had lower decision-making scores ($F=14.7$, $p<.001$). Women who were younger, had only one partner, and were categorized with androgynous sex role identity had higher relationship control scores. Women who identified as African American or Latina or who were categorized with androgynous or masculine sex role identity had higher decision-making scores.
Conclusions: Findings demonstrate partial support for multi-level predictors of gendered power among this sample. Predictors varied between the two subscales, providing additional support for the multidimensional nature of relationship power. Future HIV prevention research with drug-involved women should target multi-level factors that may affect women's heterosexual relationship power.
Financial Support: NIDA CTN U10DA13035 (E. Nunes) and NIDA K24DA022412 (E. Nunes)

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RESIDENTIAL TREATMENT SERVICES IN WEST CENTRAL MEXICO: RESOURCES AND NEEDS.

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Aims: To identify, classify and analyze residential treatment clinics in the west central part of Mexico.
Methods: We conducted an on-site survey of all residential clinics in the state of Jalisco, Mexico, investigating organizational structure, resources, facilities, accessibility, treatment orientation, length of operation, financing, grants and outreach activities.
Results: We surveyed 191 residential treatment clinics. The type was: 77 % self-help, 17 % combined medical-self help (M-SH), 5 % medical and 1 % alternative. Half of them are in Guadalajara metropolitan area and the rest around Jalisco state.One-third of the clinics have operated for less than 5 years, and one-third for 5-10 years; 44% of medical clinics have operated more than 15 years. There was substantial variation in treatment program characteristics, with only 68 % of the clinics providing a written treatment program.There was a large variation in the performing and frequency of medical and psychological evaluations among the different types of clinics. Family therapy was offered by 23 % of the self-help clinics and 56 % of the medical clinics.Specialized professional personnel was concentrated primarily in the medical clinics. Self-help groups were typically deficient in specialized personnel. Regarding public funding, 22 % of the clinics (medical and M-SH) obtained 83.6 % of the funding while 77 % (self-help) obtained only 16 %.
Conclusions: Medical and combined M-SH clinics, although not optimal, are better organized in terms of treatment programs and medical-psychological evaluations. They receive most of the public funding. Self-help clinics are the largest group offering residential treatment at very low cost but lack standard programs, medical supervision, training and funding. Greater efforts in funding, supervision and training should be devoted to this (latter) group.
Financial Support: State council for Addictions of Jalisco,CECAJ.

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A FUNCTIONALLY SELECTIVE SEROTONIN 2 RECEPTOR LIGAND FOR DRUG-INDUCED PSYCHOSES AND SCHIZOPHRENIA.

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Aims: Activation of serotonin 5-HT2 receptors (5-HT2A,2B & 2C; 5-HT2Rs) may underlie the psychotomimetic effects of hallucinogens such as (±)-2,5-dimethoxy-4-iodoamphetamine (DOI). However, antagonists of 5-HT2Rs tested for treatment of psychosis have largely been ineffective clinically. This may be due to their relatively unknown ability to effect 5-HT2R signaling through non-traditional 5-HT2R-coupled pathways, such as the phospholipase A (PLA) pathway. We developed a novel compound, CAT, an analog of the specific 5-HT2C agonist and 5-HT2A/2B antagonist, PAT, and assessed its pharmacological profile at 5-HT2Rs and its effects on the 5-HT2-dependent head-twitch response (HTR) in mice induced by DOI. We hypothesized that CAT is a functionally selective compound at 5-HT2CRs coupled to phospholipase C (PLC) and PLA signaling that may subdue drug-induced psychoses.
Methods: CAT, (1R,3S)-(–)-trans-1-cyclohexyl-3-N,N-dimethylamino-1,2,3,4-tetrahydronaphthalene, synthesis was based on the literature method for PAT. Receptor binding, 5-HT2R-coupled PLA and PLC signaling assays were performed using human 5-HT2A, 2B or 2CRs expressed in HEK293 or CHOK1 cells. DOI HTR experiments were performed as previously described (Canal et al., 2010) using adult, male C57BL/6J mice. 0.1, 1, and 3 mg/kg s.c. doses of CAT were used to test its effects on the 1 mg/kg DOI-induced HTR.
Results: CAT exhibited high affinity for the 5-HT2R family (Ki (nM) = 1.6±0.1 (5-HT2A), 23.7±0.8 (5-HT2B), 13.8±2.1 (5-HT2C)), and was an inverse agonist at each 5-HT2R linked to PLC signaling (IC50 values = 50–250 nM). Regarding 5-HT2R-associated PLA signaling, however, CAT was a potent agonist at 5-HT2CRs (EC50 = 3.0±1.7 nM). CAT produced a dose-dependent reduction, but not elimination, of the DOI-induced HTR in mice, with 3 mg/kg sc CAT reducing the DOI HTR by greater than 70% (HTR in 10 min, sal + 1 mg/kg DOI = 50, 3 mg/kg CAT + 1 mg/kg DOI = 14; $p<0.05$), without affecting locomotor activity.
Conclusions: CAT is a functionally-selective 5-HT2C ligand and may be useful as a novel medication for treating drug-induced psychoses and schizophrenia.
Financial Support: RO1 DA023928, DA030989, MH081193

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ASSESSING THE DISCRIMINATIVE STIMULUS EFFECTS OF SOMA.

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Aims: Carisoprodol (Soma®) is a centrally-acting skeletal muscle relaxant frequently prescribed for the treatment of acute musculoskeletal conditions. Recently, there has been increasing concern regarding carisoprodol's potential as a drug of abuse. Carisoprodol's mechanism of action is unclear. However, previous studies suggest carisoprodol's effects are mediated by novel modulation of the GABAAR.
Methods: Rats were trained to discriminate carisoprodol (100 mg/kg, ip) from vehicle (2% methylcellulose). The time course effect of carisoprodol was established. Rats were then tested for generalization to the muscle relaxant cyclobenzaprine and the selective GABAA agonist muscimol, which binds at the GABA site. The barbiturate antagonist bemegride and the benzodiazepine antagonist flumazenil were also tested for attenuation of the discriminative stimulus effects of carisoprodol.
Results: The discriminative stimulus effects of carisoprodol peak from 20-40 min, start to deteriorate by 80 min, and are gone by 160 minutes after administration. Cyclobenzaprine failed to substitute for carisoprodol. Bemegride dose-dependently produced rightward shifts in the carisoprodol dose effect curve, and flumazenil also attenuated the discriminative stimulus effects of carisoprodol.
Conclusions: The discriminative stimulus effects of 100 mg/kg carisoprodol have a fairly slow onset and a moderate duration of action which parallels the time course of its locomotor depressant effects. Carisoprodol produces its discriminative stimulus effects at the GABAA receptor. Both the barbiturate and the benzodiazepine sites may be involved. Whether other receptors or sites are important is not yet clear.
Financial Support: NIH R01DA022370

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EVIDENCE OF PREFERENCE FOR HIGHER SUCROSE SOLUTIONS IN PSYCHOACTIVE SUBSTANCE SUBJECTS.

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Aims: Human and animal studies suggest that alcoholics and cocaine users prefer high concentration sweet solutions or sweet substances. The aim of this study was to evaluate the preference for higher sucrose concentration in psychoactive substance users.
Methods: A convenience sample of 110 individuals (74% men, mean age 35±12yrs, 43% filled DSM-IV criteria for psychoactive substance addiction: 40% marijuana dependence, 48% cocaine dependence, 55% alcohol dependence, 43% tobacco dependence. They responded to a questionnaire on sugar and other psychoactive substances and tasted for three times solutions with 0.05, 0.21 and 0.83 M sucrose concentrations. They were subsequently asked to rate their degree of preference for, and the degree of sweetness of each solution. Data were collected in Brazilian substance addiction treatment centers and analyzed by bivariate analysis.
Results: Psychoactive substance dependent subjects prefer more frequently the highest sucrose solution (0.83M) than non-dependents (55% vs. 23%; $p<0.01$). We found the same results for each individual psychoactive substance: marijuana (67% vs. 33%; $p<0.01$); cocaine (62% vs. 28%; $p<0.01$), alcohol (57% vs. 30%; $p<0.01$) and tobacco (55% vs. 36%; $p<0.05$). Individuals with more than two concomitant substance addictions prefer the highest sucrose solution (61% vs. 39%; $p<0.01$).
Conclusions: The results of this study showed that individuals with psychoactive substance had a preference for high concentrations of sucrose, which it is more frequent in individuals with polysubstance dependence. The association between sweet preference and psychoactive substances intake may be determined by a common mechanism mediating the rewarding properties of both sweets and psychoactive substances, such as the brain opioid system.
Financial Support: CNPq; FAPEMIG

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SMOKING, ALCOHOL, DRUGS AND DELINQUENCY AMONG HIGH SCHOOL STUDENTS IN CAPE TOWN, SOUTH AFRICA.

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Aims: To examine the relationship between alcohol, tobacco and drug use and delinquent behaviors among high school students and identify potential confounders.
Methods: Secondary data analysis was conducted on longitudinal data collected from students in Cape Town high schools at three different time periods. The participants completed a self-report questionnaire which measured a number of risk factors including lifetime use of alcohol, tobacco and other drugs, delinquent behaviors, as well as demographic factors. Several variables measuring delinquent behaviour were used to construct a composite measure of delinquency. This was the outcome variable of interest. Logistic regression was used to compare the relationship between risk and predictive factors and delinquency, after weighting for dropout.
Results: At Time 1, 1470 students participated, at Time 2, there were 856 participants and by Time 3, 491 participants remained. After adjusting for dropout, logistic regression results indicated that at Time 1, drug use (AOR: 2.74, CI: 1.58-4.75), alcohol (AOR: 3.17, CI: 2.19-4.60) and smoking (AOR: 1.68, CI: 1.19-2.36) were significant predictors of delinquency. At Time 2, alcohol (AOR: 2.21, CI: 1.49-3.29) and drug use (AOR: 1.88, CI: 1.49-3.29) were significant predictors of delinquent behavior. At Time 3, drug use (AOR: 1.62, CI: 1.04-2.49) remained a significant predictor and while alcohol was not significantly related to delinquent behavior, smoking re-entered the model (AOR: 1.62, CI: 1.04-2.52). Gender, race and socioeconomic status significantly confounded the relationship of interest at different times in the study.
Conclusions: Drug use is clearly associated with delinquent behavior. Intervention efforts aimed at at-risk adolescents in high schools should include substance use and delinquency, and may need to be tailored for different subgroups.
Financial Support: None

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COUNSELOR CHARACTERISTICS INFLUENCE MI SKILL ACQUISITION FOLLOWING WORKSHOP AND POST-WORKSHOP TRAINING.

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Aims: To test the relationship between counselors' occupational, educational, and cognitive characteristics and the acquisition of motivational interviewing (MI) counseling skills before and after formal training.
Methods: Fifty-eight community-based counselors completed a 2-day MI workshop and were randomly assigned to a post workshop MI supervision condition (i.e., teleconferencing, tape-based, or workshop only). Audio-taped clinical encounters were rated for MI skillfulness at four time points (pre-workshop and 1, 8, and 16 weeks post workshop). The relationships between counselor characteristics and MI skills before and after workshop training were tested with zero-order correlations and linear regressions, respectively. Generalized linear mixed effect models were used to assess: 1)the effects of supervision conditions on MI skills over time, and 2)the potential modifications of these effects by counselor characteristics.
Results: Higher estimates of intelligence ($r=0.34$; $p < .01$) and more years of professional experience ($r=0.33$; $p < .01$) were associated with stronger MI skills before workshop training. Counselors with more professional experience demonstrated greater changes in MI skills immediately following workshop training ($\Delta R2 = .10$, $F(1,51) = 7.80$; $p <.01$). The effects of different post workshop supervision procedures were moderated by characteristics of the counselors. Specifically, live coaching and feedback were most effective for increasing the ratio of complex reflections to questions among counselors with a graduate education ($F(6,26) =3.03$; $p=.03$) and stronger verbal and abstract reasoning abilities ($F(2,26) =3.45$; $p=.05$), and for increasing empathy ratings among counselors with lower abstract reasoning skills ($F(2,25) =9.85$; $p < .001$).
Conclusions: Training programs for increasing MI counseling skills may be differentially effective depending upon the cognitive skills, as well as the professional and educational experience of prospective trainees.
Financial Support: NIDA grants R01 01695 and K23 021850.

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PSYCHOLOGICAL FACTORS ARE ASSOCIATED WITH STIMULANT USE IN A PROBABILITY-BASED SAMPLE OF URBAN MSM.

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Aims: Stimulant (i.e., cocaine, crack, and methamphetamine) use has negative implications across the spectrum of HIV prevention and care. Prior studies examining psychological correlates of stimulant use recruited convenience samples of active methamphetamine users, which substantially limits generalizability. The present study examined psychological correlates of stimulant use in urban men who have sex with men (MSM) recruited through probability-based sampling.
Methods: The 2002 Urban Men's Health Study obtained a household probability sample of 879 MSM residing in San Francisco using random digit dialing from May of 2002 through January of 2003. Of these, 711 (81%) completed a mail-in survey that assessed psychological factors and substance use in the last 6 months. Using multiple logistic regression, we examined psychological correlates of engaging in any stimulant use after adjusting for age, education, income, and ethnicity.
Results: Most participants were HIV-negative (72%), middle-aged ($M = 44$, $SD = 11$), Caucasian (85%), and had at least a 4-year college degree (69%). Because HIV-positive MSM had greater odds of reporting stimulant use (OR = 1.80, 95% CI = 1.21 – 2.51), stratified analyses were conducted. Among HIV-negative MSM (n = 519), depressive symptoms (Adjusted OR [AOR] = 1.42, 95% CI = 1.08 – 1.87) and sexual compulsivity (AOR = 1.37, 95% CI = 1.01 – 1.85) were independently associated with increased odds of stimulant use. Conversely, HIV-specific anxiety was independently associated with decreased odds of stimulant use (AOR = 0.66, 95% CI = 0.50 – 0.86). Among HIV-positive MSM (n = 192), sexual compulsivity was independently associated with greater odds of stimulant use (AOR = 1.61, 95% CI = 1.11 – 2.34).
Conclusions: Psychological interventions targeting sexual compulsivity and depression could reduce stimulant use in the broader population of MSM, many of whom never present for formal substance abuse treatment.
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ESCALATION AND REINSTATEMENT OF STIMULANT SEEKING IN ADOLESCENT AND ADULT RATS.

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Aims: Adolescents are more likely than adults to initiate and maintain drug abuse leading to life-long drug problems, impulsivity, and externalizing disorders. The purpose of these studies was to compare adolescent and adult rats that were selectively bred for high (HiS) or low (LoS) saccharin intake using two animal models of critical phases of drug abuse - bingeing and reinstatement.
Methods: EXP 1: ESCALATION. Adolescent (postnatal day – PND 23) and adult (PND 90) male rats self-administered methamphetamine (METH) infusions (0.05 mg/kg) during short (ShA-2 h)- or long (LgA-6 h)- access sessions for 16 days. The four groups were compared on the number of responses and infusions and their rate of escalation over the 16 days. EXP 2: REINSTATEMENT. Four groups of female rats were compared on cocaine-, stress, and cue-primed reinstatement of cocaine seeking. The groups were adolescent or adult rats bred for high (HiS) or low (LoS) saccharin intake with corresponding high and low vulnerability to drug abuse.
Results: EXP 1: ESCALATION. In the LgA (6 h) groups, adolescents self-administered more METH than adults, and both groups showed an escalation effect. In contrast, the ShA (2 h) adolescent and adult rats earned a similar number of METH infusions and showed no escalation of intake. EXP 2: REINSTATEMENT. During the cocaine maintenance phase, HiS adolescent rats self-administered more cocaine than HiS adults. There were no age differences in LoS rats during maintenance or HiS/LoS differences during extinction. Both HiS and LoS adolescents showed higher cocaine-primed reinstatement than their adult counterparts. There were no age or HiS/LoS differences in cue- or stress-primed reinstatement.
Conclusions: Adolescent rats exceeded adults on the escalation of cocaine intake during LgA and cocaine-primed reinstatement. Adolescence interacted with the HiS phenotype to produce the highest reinstatement. Enhanced drug seeking in adolescents vs. adults was consistent across METH and cocaine, males and females, and HiS and LoS rats.
Financial Support: Supported by NIDA grants: R01 DA003240, R01 DA019942, and K05 DA015267 (MEC).

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COMPARISON OF DSM-IV AND PROPOSED DSM-5 SUBSTANCE USE DISORDER CRITERIA IN US ADOLESCENTS.

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Aims: Revisions to substance use disorder diagnosis proposed in DSM-5 include: (1) eliminating the distinction between abuse and dependence and the legal problem criterion; and (2) introducing a craving criterion. We compared DSM-IV and proposed DSM-5 criteria in a community based sample of adolescents.
Methods: Subjects were drawn from the National Comorbidity Survey-Adolescent Supplement, a representative survey of 10,123 US adolescents aged 13-18 years. DSM-IV and proposed DSM-5 drug and alcohol use disorders were assessed using a modified version of the WHO Composite International Diagnostic Interview. Symptom and disorder prevalances and κ values of concordance between DSM-IV and -5 disorders were estimated and predictors of discordance were modeled in logistic regression.
Results: Lifetime and 12 month prevalence estimates of DSM-5 substance use disorders were 10.3% (95% confidence interval 8.9-11.9) and 7.6% (6.6-8.8) respectively, versus DSM-IV prevalence estimates of 11.5% (10.1-13.1) and 8.5% (7.5-9.6). Lifetime prevalence of legal problems due to drug or alcohol use (1.7%) was lower than other DSM-IV or -5 symptoms (range 2.2%-11.0%), while craving prevalence (3.0%) was comparable to that of other symptoms. Lifetime DSM-IV/5 concordance (κ) was .89 overall and ranged from .63 for alcohol to .99 for cocaine. Older, white, non-Hispanic adolescents were most likely to receive discordant diagnoses, as were youth reporting legal problems from use.
Conclusions: In US adolescents, proposed DSM-5 substance use disorder prevalence are similar to DSM-IV rates and identify largely the same cases. Findings support the rationale for proposed criteria revisions.
Financial Support: American Academy of Child & Adolescent Psychiatry and National Institute on Drug Abuse (K12 DA000357); National Institute of Mental Health (U01 MH60220); National Institute on Drug Abuse (R01 DA016558); Intramural Research Program, National Institute of Mental Health

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USE OF OVER-THE-COUNTER CODEINE IN AUSTRALIA.

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Aims: To investigate trends in the use of OTC codeine amongst a sample of people who inject drugs regularly; and to investigate the pain and non-pain reasons for using OTC codeine.
Methods: In June 2010 face to face interviews were conducted with 902 people who inject drugs regularly (PWID).
Results: In 2010, 35% percent reported using OTC codeine in the last six months. The median number of tablets/capsules taken at one time was three, range 1-250. The median dosage the last time they took OTC codeine was 26mg of codeine. One participant reported using more than 100 tablets in a session. Fifty-two percent of users took more than the recommended dose (2 tablets) last time they took OTC codeine. The most common non-pain reasons for codeine use were to go to sleep and to substitute for heroin or illicit opioids.
Conclusions: The high number of OTC codeine users taking above the recommended dose of codeine combination drugs (paracetamol and ibuprofen) indicates this group could be at risk of adverse events associated with these medications.
Financial Support: Funded by the Australian Department of Health and Ageing

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RISK-TAKING: INFLUENCE OF TOBACCO USE AND PEERS.

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Aims: A variety of high risk behaviors including tobacco use are initiated during adolescence, and peer pressure has been shown to play a major role in the initiation of these behaviors. We were interested in examining the interaction of tobacco use and peer pressure on responses on the Balloon Analogue Risk Task (BART).
Methods: The BART was modified to include a peer components and the impact of peer influences on risk taking behavior was examined in adolescent smokers and nonsmokers. 39 adolescents (22 smokers, 17 nonsmokers) recruited from high schools in CT completed one experimental session during which the regular- and peer-BART were presented in counterbalanced order.
Results: Smokers reported smoking 15.1 cigs/day (SD = 4.9) and had modified FTQ scores of 5.6 (SD =1.8). Results from a repeated measures ANOVA showed significant increases in the number of explosions in response to the peer BART when compared with the regular BART ($F(1, 39) = 6.96$, $p = .01$) with no significant changes in adjusted average pumps ($p=0.09$). The changes in risk-taking in response to the peer BART differed by smoking status ($F(1, 39) = 4.14$, $p = .05$); specifically smokers had greater increase in the number of explosions by 2.27 (SD = 3.12) compared to an increase of .29 (SD = 2.87) by non-smokers. While no correlations were found between peer-influenced changes in risk-taking on the BART and resistance to peer influence (RPI, Steinberg and Monahan, 2007), positive correlations were observed with trait impulsivity measures (BIS-11, Barratt, 1959) for total scores ($r=0.45$, $p<0.05$) as well as the subscales of non-planning impulsivity ($r=0.35$, $p<0.05$) and cognitive impulsivity ($r=0.50$, $p<0.01$).
Conclusions: These results suggest that adolescent smokers, especially those who are more impulsive, are more susceptible to peer-influences on risk-taking behavior. These findings have important implications for the development of optimal prevention and cessation programs for risky behaviors among adolescents.
Financial Support: Supported by P50 DA09241

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PREGNANT BY AGE 15 AND SUBSTANCE USE INITIATION AMONG U.S. ADOLESCENT FEMALES.

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Aims: To examine onset of substance use across multiple substances (alcohol, cigarettes, and marijuana) and associations with likelihood for teenage pregnancy by age 15.
Methods: Participants were adolescent girls ages 15 or younger (weighted n = 5,825) who participated in the 1999-2003 Youth Risk Behavior Surveillance System (YRBSS), a cross-sectional, nationally representative survey. Multivariable logistic regression was used to examine associations between having been pregnant as a function of age of substance use initiation (i.e., age 10 or younger, 11 – 12, 13 – 14, and age 15) for alcohol, cigarettes and marijuana, while controlling for race/ethnicity and metropolitan location.
Results: Three percent (weighted n = 174) of the girls in our sample had experienced a pregnancy and the majority of these girls had already initiated alcohol, cigarettes, and marijuana use by age 15. In multivariable analysis marijuana initiation at any age increased the likelihood of experiencing a pregnancy by age 15 (odds ratios ranged from 3.1 to 11.3). Girls who initiated cigarette smoking at age 12 or younger were also significantly more likely to have experienced a pregnancy by age 15 (odds ratios ranged from 3.0 to 4.3). No significant associations were found between initiation of alcohol use and very early teenage pregnancy.
Conclusions: Marijuana use at any age and/or cigarette smoking by age 12 better characterize young girls who appear to have a problem-prone trajectory into pregnancy by age 15. This could be due to a common underlying risk factor and is cause for concern given the detrimental health consequences for offspring that stem from maternal smoking behaviors.
Financial Support: PC: UL1 RR024992 and KL2 RR024994 from NCRR and NIH Roadmap for Medical Research, NIDA, K01DA025733. LB: NIH Midcareer Investigator Award (K02 DA021237). LC: NIDA grant 5 T32 DA07313-09.

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HIV SERO-STATUS, KNOWLEDGE, AND INJECTION BEHAVIORS AMONG METHADONE MAINTENANCE TREATMENT CLIENTS IN URBAN VS. RURAL SETTINGS OF KUNMING, YUNNAN.

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Aims: The purposes of this study are: (1) to document the prevalence of Human Immunodeficiency Virus (HIV) among methadone maintenance treatment (MMT) clients in urban and rural settings of Kunming city, Yunnan province, China; (2) to examine differences in HIV knowledge and injection behaviors among this population residing in different geographic areas.
Methods: Using data collected from 160 patients admitted from 2009 to 2010 in two MMT clinics, we compared clients attending urban versus rural clinics of Kunming city concerning their sero-status and knowledge about HIV, and their injection behaviors.
Results: Urban MMT clients were younger, more held jobs, more reported prior arrest, and had better social supports as compared to their rural counterparts. The HIV seropositive rates were 10.0% in urban and 27.7% in rural clinics. Clients scored on average fewer than 19 correct out of the 45 items in the HIV knowledge questionnaire, while no difference was found between clients in two clinics. Reported drug injection in the past 30 days was 44.8% in urban and 65.5% in rural clients. Reported recent injection and different geographic area were strong predictors of these clients' HIV status.
Conclusions: The lack of knowledge about HIV infection, transmission, and treatment among both urban and rural MMT clients suggest the need to strengthen current HIV education programs in MMT clinics. In addition, HIV prevention programs should take into consideration characteristics of the target population in specific geographic areas.
Financial Support: Supported by NIDA R21 DA025252, P30DA016383, & K05DA017648 (PI: Hser)

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COMPARATIVE GENE EXPRESSION PROFILING ANALYSIS OF LYMPHOBLASTOID CELLS IN HEROIN ADDICTS.

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Aims: Heroin addiction is a chronic mental disorder with a high relapse rate and a high genetic predisposition. The aim of study was to investigate the genetic underpinnings of heroin addiction.
Methods: We compared the total gene expression profiles of lymphoblastoid cells between 20 male heroin addicts and 20 male controls using an oligonucleotide-based total gene expression microarray, and conducted pathway analysis of the differentially expressed genes between two groups. We also verified the differential expression of several selected genes in expanded sample sizes using real-time quantitative PCR.
Results: We identified 870 differentially expressed gene transcripts between heroin addicts and control subjects, including 262 up-regulated and 608 down-regulated gene transcripts. Further pathway analysis of these differentially expressed gene transcripts revealed several genetic pathways associated with heroin addiction, including the T cell receptor signaling pathway.
Conclusions: Our data support the idea that heroin addiction is a complex genetic disorder with involvement of polygenes and several perturbed pathways. The differentially expressed genes can be considered as candidate genes for heroin addiction when looking for genetic variants associated with heroin addiction, and the perturbed pathways can bring new insight into the pathogenesis of heroin addiction in future studies.
Financial Support: The study was supported by grants from the National Science Council, Taiwan, and the National Health Research Institutes, Taiwan.

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RELATIONSHIP BETWEEN PUBERTAL DEVELOPMENT AND ALCOHOL EXPECTATION IN LATE CHILDHOOD.

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Aims: With a focus on late childhood- a critical period for transition into underage and problematic drinking, the aim of the study is to investigate the extent to which puberty development influences the endorsement of alcohol expectancies by gender.
Methods: A representative sample 391 boys and 395 girls from 16 public schools in the urban region in Taiwan were first assessed in 4th grade (mean age=10) and followed-up annually till 6th grade. Information was collected via self-administered paper-and-pencil questionnaires, incluidng Self-Rating Scale for Pubertal Development and the Alcohol Expectancy Questionnaire-Children version that has three positive (eg,enhanced social behaviors, ESB) and one negative domain (ie,deteriorated cognitive and behavioral functions, DCBF). Two-level generalized latent and mixed models were performed to evaluate gender-specific relationships while accounting for the complex survey design.
Results: An estimated 31% boys and 24% girls had tried alcohol on at least one occasion prior to the age of 10; and the corresponding estimates are 49.2% and 45.8% respectively in 6th grade. With adjustment for age and family characteristics, early alcohol initiation was significantly related to the endorsement of ESB (β: boys= 1.48, girls=1.03) and DCBF (β: boys: 0.90, girls=-0.69) from 4th onward to 6th grade. With adjustment for intra-individual changes in current alcohol drinking, we found a relationship between puberty development with positive and negative alcohol expectancies only in girls.
Conclusions: Early-onset alcohol initiation, but not current alcohol drinking, was related with elevated positive alcohol expectancies; in age 11-12, the effects of early pubertal development on the endorsement of alcohol expectancy were only salient in girls. This evidence may provide some etiological and preventive implications for alcohol drinking problems in adolescence.
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CORRELATES OF ILLICIT DRUGS USE AND NONMEDICAL USE OF ADDERALL® IN THE UNITED STATES.

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Aims: Adderall® has one of the highest potential for dependence or abuse among the group of legally approved drugs. This study uses data from 2008 National Survey on Drug Use and Health (NSDUH) to describe the socio-demographic characteristics of its users and to examine the relationship between nonmedical use of Adderall® and other illicit drugs use.
Methods: Participants were 55,739 non-institutionalized civilians aged 12 years and older from the 2008 NSDUH. Frequency distribution was used to describe the socio-demographic correlates of nonmedical use of Adderall®. Logistic regression was used to examine the association between nonmedical Adderall® use and aspects of other illegal drugs involvement.
Results: We found that among the group of past-year nonmedical use of Adderall®, 55.2% are male and 44.8% are female. The frequency distribution is significantly higher in age group of 18-25 (58.7%). The main users are largely White (84.9%), and more than half of them have attended college (53.2%). The rate of Adderall® nonmedical use is highest in low-to-moderate household income (58.9%). Multiple logistic regression findings revealed that nonmedical use of Adderall® has no correlations with other illicit drugs use, such as marijuana (aOR:1.05 [95%CI:1.01-1.08]), methamphetamine (aOR:0.83 [95%CI:0.78-1.14]), cocaine (aOR:1.04 [95%CI:0.98-1.10]), heroin (aOR:1.04[95%CI:0.99-1.09]), and LSD (aOR:0.84 [95%CI:0.78-1.10]).
Conclusions: The findings suggest that the nonmedical users of Adderall® are mainly young, Caucasian, and have college level education or above. Nonmedical use of Adderall® is not strongly correlated with other substances use, including CNS stimulants. The socio-demographic data and its correlates with other illicit drugs can lend insight for policy makers for abuse prevention.
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BURDEN OF SUBSTANCE ABUSE IN ELDERLY PROSTATE CANCER PATIENTS.

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Aims: To analyze the predictors and the incremental burden of substance abuse in elderly prostate cancer patients.
Methods: We used SEER-Medicare linked database between 1995 and 2003. From a cohort of men diagnosed with prostate cancer between 1995 and 1998, we identified those with a diagnosis of substance use (ICD-9: 303.xx, 304.xx, 305.xx) during treatment phase (one year post-diagnosis) or follow-up phase (4 years post-treatment phase). Logistic regression was used to analyze the predictors of substance abuse. GLM log-link model was used to assess the incremental cost of substance abuse in treatment and follow-up phase. We used Cox regression to assess the hazard of mortality associated with substance abuse in treatment and follow-up phase.
Results: Of the 50,147 men newly diagnosed for prostate cancer, 2.14% had a diagnosis of substance use in treatment phase and 5.36% had a diagnosis of substance use in follow-up phase. Older age (Odds Ratio (OR)=0.98, 95% Confidence Interval (CI) =0.94, 0.96) and being married (OR=0.67, CI=0.62, 0.72) was associated with lower odds of substance abuse. Surgery (OR=1.18, CI=1.06, 1.3), African American ethnicity (OR=1.34, CI=1.22, 1.47) and higher TNM stage (OR=1.25, CI=1.15, 1.36) were associated with higher odds of substance abuse. The incremental cost of substance abuse was 29% in treatment phase and 69% in follow-up phase. Substance abuse in treatment phase had higher hazard of all-cause mortality (hazards ratio (HR) = 2.6; 95% Confidence Interval (CI) = 2.4–3.1).
Conclusions: A co-occurring diagnosis of substance abuse appears to exert higher burden of cost and mortality among elderly prostate cancer patients. This emphasizes the need for further research to study the effects early diagnosis and treatment of substance abuse in elderly prostate cancer patients.
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CHANGES IN PROBLEM DRUG BEHAVIOR AMONG NONMEDICAL OXYCONTIN USERS.

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Aims: Development of interventions to reduce the public health burden of abuse of OxyContin® (oxycodone controlled-release) and other prescription opioids, including formulations with abuse-deterrent features, requires an understanding of drug using behaviors of nonmedical users. This study aims to assess changes over time in opioid dependence, heroin use, and injecting drug use, among nonmedical users of OxyContin and other prescription opioids.
Methods: Data from the 2004 to 2008 National Survey on Drug Use and Health (NSDUH) public use datasets were used to estimate the prevalence of nonmedical use of OxyContin and other prescription opioids for each year of the survey. Among those who reported nonmedical use of OxyContin and other opioids in the past year, prevalence of past year heroin use, opioid dependence, and history of injecting drug use were estimated.
Results: Trends in nonmedical use of OxyContin and other prescription opioids were relatively stable from 2004 to 2008. In 2004, OxyContin users were three times more likely than those using other opioids to be opioid dependent (24.3% vs. 8.8%), six times more likely to have used heroin in the past year (11.4% vs. 1.9%) and twice as likely to have injected drugs (14.3% vs. 6.7%). In addition, these problem drug behaviors became more prevalent among nonmedical OxyContin users over time. Compared to 2004, in 2008 there was a 31% increase in the prevalence of opioid dependence (from 24.3% to 31.8%) and a 74% increase in history of drug injecting (from 14.3% to 24.9%). Frequency of nonmedical OxyContin use also increased during this period.
Conclusions: Although prevalence of nonmedical OxyContin use did not increase significantly from 2004 to 2008, there was an increase in problem drug behaviors among its users. There are many possible explanations for these findings; however, interventions targeting opioid abuse in general and OxyContin in particular need to consider these results. These data will serve as a baseline for observing the effects of a new formulation of OxyContin.
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"UNSEEN" VULNERABILITY: COCAINE RELAPSE IS ASSOCIATED WITH LIMBIC ACTIVATION TO DRUG CUES PRESENTED OUTSIDE AWARENESS.

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Aims: Our laboratory has shown that even "unseen" (backward-masked) 33 msec cocaine cues can activate limbic motivational circuitry in cocaine patients. Linking these brain findings to addiction-relevant outcomes (e.g., drug use/relapse) is critical for determining their ultimate clinical significance. We hypothesized that individuals who relapse would evidence limbic activation to "unseen" cues – and that individuals without relapse might not evidence this response.
Methods: In a "fast" event-related BOLD fMRI paradigm, cocaine patients were exposed to cocaine-related and to comparison (sexual, aversive and neutral) cues of 33 msec duration. Each cue (24 stimuli per category) was "backward-masked" by a 467 msec neutral stimulus to prevent conscious recognition. Pre-planned contrasts were calculated within SPM 2 for patients dichotomized on drug use outcomes during 8 weeks of outpatient treatment: "Relapse", 4 or more consecutive cocaine-positive urines (n=17), and "No Relapse"(n=8).
Results: Cocaine patients who relapsed evidenced a robust response to "unseen" cocaine cues in limbic regions of interest (e.g., lateral amygdala, bilateral insula, v. striatum/v. pallidum, p<.000; t range 2 to 10), while patients who did not meet relapse criteria entirely lacked this differential cue reactivity.
Conclusions: These data provide direct evidence that the limbic brain response to "unseen" drug cues has clinical significance, as it is associated with cocaine relapse. These findings characterize a "cue-vulnerable" endophenotype for which conventional (conscious) psychosocial interventions may have limited effectiveness – and for which brain-targeted pharmacotherapies may be especially important. The "unseen" cue paradigm may be useful both as a tool for screening anti-relapse medications, and for identifying the "cue-vulnerable" patients who need these medications most.
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CIGARETTE SMOKING AND NEONATAL ABSTINENCE SYNDROME IN OPIOID-DEPENDENT AGONIST-MAINTAINED PREGNANT PATIENTS ON METHADONE VS. BUPRENORPHINE.

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Aims: To examine the association between cigarette smoking and neonatal abstinence syndrome (NAS) pharmacologic treatment among agonist-maintained pregnant patients on methadone v. buprenorphine.
Methods: Participants were N=119 agonist-maintained pregnant women selected from 131 opioid-dependent pregnant patients who completed a multi-site randomized controlled, double-blind, double-dummy intervention trial of methadone v. buprenorphine.
Results: The association between smoking and NAS pharmacologic treatment differed between methadone and buprenorphine groups. Among buprenorphine patients, each additional cigarette per day (CPD) smoked with two weeks of delivery increased the odds of NAS treatment by 31% [OR:1.31; 95%CI:(1.07 - 1.59); p-value=0.008]. This association was not observed in the methadone group, and no statistically significant association between average CPD and NAS treatment was observed among either methadone or buprenorphine patients [OR:1.05; 95%CI:(0.944 – 1.16); p-value=0.383]. Among buprenorphine patients, the relationship between CPD near delivery and NAS treatment was attenuated by maternal depression and illicit drug use.
Conclusions: Further investigations are needed to clarify the complex relationships among smoking, opioid-treatment, and NAS.
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LONG-TERM STABLE ABSTINENCE IN ADULTS WHO USED METHAMPHETAMINE.

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Aims: Limited information is available on long-term addiction recovery among adults who used methamphetamine (meth). The aim of this study is to identify predictors of stable abstinence from substance use during an 8-year period in the "meth use career," beginning an average of 15 years after meth use initiation.
Methods: Data are from an intensive natural history study of meth users in Los Angeles county (N=255); 65% received substance abuse treatment in the mid-1990s. Respondents were interviewed in 2001-03, and approximately 8 years later in 2009-10. Those who reported continuous abstinence from alcohol and illicit drug use since the earlier interview (5%) were compared to respondents with 2-7 years of abstinence (9%) and a non-abstinent group with use in the most recent 2 years (86%). Demographic, substance use history, treatment, self-help and mental health variables were explored by abstinence status using chi square and GLM.
Results: Preliminary results indicate the abstinent and non-abstinent groups did not differ by gender, race, education or substance use history. The 8-year abstinent group was more likely to be employed and married compared to other groups ($p<.05$). The abstinent groups had lower levels of depressive symptoms and rated the importance of spirituality more highly than the non-abstinent group ($p<.05$). A higher rate of those who received treatment in the mid 1990s were in the abstinent groups compared to those not treated; 70% of the 2-year abstinent group, and 32% of the non-abstinent group received treatment since the last interview. Two-thirds of the abstinent groups participated in 12-step meetings compared to 20% of the non-abstinent group ($p<.001$).
Conclusions: Although few meth users achieved stable abstinence, these findings suggest that in addition to timely treatment, addressing depressive symptomatology may enhance the likelihood of achieving stable recovery. Former meth users with long periods of abstinence are continuing to participate in self help, indicating the importance of this resource in maintaining stable abstinence.
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EXERCISE AS A NOVEL APPROACH TO METHAMPHETAMINE TREATMENT.

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Aims: Methamphetamine (MA) abuse continues to be a significant problem. Exercise has proven effective in treating various other medical and psychiatric conditions. The overall objective of this study is to provide foundational information on the utility and efficacy of an 8-week progressive aerobic and resistance exercise training program on mood and post-treatment MA use. Data presented here are preliminary and part of an ongoing study.
Methods: Twenty-one residential MA-dependent individuals were randomized to 3 d/wk of exercise training (EX, n=11) or health education (ED, n=10) over an 8-wk study period. Mood was assessed using the BDI, BAI, POMS, and Daily Mood Rating at baseline (BL), weekly, and at intervention completion (Wk 8). Aerobic fitness, body composition, muscle strength and endurance were assessed at BL, and Wk 8.
Results: Both groups showed significant ($p<.05$) decreases in mean BAI, BDI, POMS scores from BL to Wk 8. Mean BAI score for EX grp (10.8 to 1.14), ED grp: (16.6 to 5.9); Mean BDI score for EX: (14.05 to 9.86), ED: (15.2 to 8.6); Mean POMS Total Mood Disturbance for EX: (46.3 to 26.4), ED: (62.7 to 35.6). On a Daily Mood Rating taken after each session, participants in the EX grp reported feeling more euphoric ($p=.05$) and a decrease in craving ($p<.05$) from BL to Wk 8 while the ED grp did not show any significant changes from BL to Wk 8. With regard to physiological measures, participants in the EX grp significantly ($p<.05$) increased oxygen uptake (38%), muscle strength (chest=51%; legs=38%) and endurance (chest=56%; legs=76%), and showed a reduction in body weight (2%), fat weight (26%), and percent relative body fat (23%) from BL to Wk 8. The ED grp did not show any significant changes in the above variables from BL to Wk 8.
Conclusions: Although these results are preliminary, this is the first known study to report the psychological and physiological effects of 8-wks of exercise training on MA-dependent individuals. The impact of exercise on recovery from MA-dependency remains to be elucidated in this ongoing study.
Financial Support: DA027633

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AGE-RELATED CHANGES IN THE PATTERNS OF DIVERSION OF PRESCRIPTION OPIOIDS IN 18-75 YEAR OLDS ENTERING DRUG TREATMENT PROGRAMS.

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Aims: There have been very few systematic studies of age-related changes in the patterns and characteristics of the misuse of opioids. In this study we sought to determine whether the means by which opioids were diverted from therapeutic channels was influenced by age.
Methods: We recruited 2,226 patients, aged 18-75, from treatment programs across the nation to complete an anonymous survey examining patterns of drug diversion and misuse.
Results: With increasing age, patients, particularly women, became much less risk-averse than their younger counterparts in the mode of drug diversion. While doctor's prescriptions were rarely the primary source of opioids (<10%) of 18-24 year olds, legitimate medical channels were used four times more often by those over 45. The use of dealers showed precisely the opposite relationship being used extensively by young patients but much less often in men and, particularly women, over the age of 45. Theft and forged prescriptions were rarely used (<3%) in aging addicts. These age-related changes in source translated into the selection of a primary drug. Older patients favored medications relatively easily available from a doctor (methadone or hydrocodone), for pain, whereas 60% of younger patients used dealers to obtain primary drugs less likely to be freely accessible from a doctor (e.g. ER oxycodone).
Conclusions: Our results suggest that "one-size fits all" treatment, intervention and prevention programs are unlikely to succeed given the stark differences between misuse in adolescent/young adults and more elderly ones. One of the major differences is that efforts to decrease diversion must focus on different targets in young vs. older prescription opioid misusers.
Financial Support: This research was supported by grants DA21330 and DA020791-01.

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SEX AND RACIAL DIFFERENCES IN VICTIMS OF SEXUAL ABUSE IN A COMMUNITY CORRECTIONS POPULATION.

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Aims: The purpose of this study was to examine how victims of sexual abuse in a community corrections population differ as a result of their sex and race.
Methods: Of the 19,659 participants, a total of 1,306 (6.6%) reported a history of sexual abuse and were compared to non-abused participants. The sample was analyzed by race-gender groups (White males, White females, Black males, and Black females) using univariate and logistic regression analyses, which were conducted separately for each group.
Results: White women were the most likely to report a history of sexual abuse (26.5%), followed by Black women (16%), White males (4.0%), and Black males (1.1%). For all groups, histories of suicidal ideation and suicide attempts were associated with a history of sexual abuse. Sexual abuse was associated with substance abuse problems for females, but not the males. Cannabis Dependence was associated with sexual abuse for the White women while Cocaine Dependence was associated with sexual abuse for the Black women. Several other variables were associated with sexual abuse for women, but not men, including lower education (White women only), a history of violent offenses (White women only), and living in a shelter (Black women only). Black males tended to have higher levels of education; this was the only variable uniquely associated with either male group. Receiving psychiatric medications was associated with sexual abuse for all groups except Black men and a history of sex for drugs was associated with sexual abuse for all groups except White men.
Conclusions: Consistent with national sample, women, particularly White women, were more likely to be victims of sexual abuse. The gender-race differences for the sociodemographic factors associated with sexual abuse, particularly the risk of substance abuse for women, suggest the need for tailored interventions for sexual abuse prevention and treatment.
Financial Support: Supported by UAB Psychiatry Departmental Funds.

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LEVEL OF CRIME PREDICTS DIFFERENTIAL MORTALITY RISK PRIOR TO OPIOID MAINTENANCE TREATMENT.

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Aims: Provision of opioid maintenance treatment (OMT) is the main strategy to reduce mortality in heroin dependent persons. Do all OMT applicants benefit equally from OMT? Or, would risk of mortality in patients with different levels of criminal activity prior to treatment entry vary?
The aim of this papers is to investigate whether varying levels of criminal activity prior to treatment predicted mortality levels and treatment response in patients in OMT, in order to identify different risk profiles.
Methods: Heroin dependent persons from a national cohort including all persons applying for OMT in Norway (1997-2003) were included. The complete national patient registry (n=3299) was linked with national crime-statistics, including dates of death among deceased persons (n=161). Three levels of crime during the 3 years prior to treatment-application was established based on numbers of criminal charges; No crime (0), low crime (1-25) and high crime (10% most criminally active) (26 or more). Mortality is expressed as all-cause rates per 100 person years.
Results: The three different crime-intensities 3 years prior to application predicted different mortality rates at waiting list for OMT; no-crime (2.9 [2.5-3.3]), low-crime (2.4 [2.1-2.7]) and high-crime (6.0 [5.5-6.5]). However, all 3 crime-level groups showed similar mortality rates while in OMT; no-crime (1.2 [0.9-1.6]), low-crime (1.4 [1.1-1.7]) and high crime (0.9 [0-1.5]).
Conclusions: The high-crime group had the largest reduction (to 1/6) in mortality from the pre-treatment level, and hence represents those that benefited most from OMT in terms of reduced risk of mortality. All groups had significant crime reductions during OMT, but the no-crime and low-crime groups showed around 50% reduction in mortality risk. Those highly criminally active prior to treatment, sometimes considered by clinicians as the "more problematic OMT-applicants", in particular need prompt treatment acceptance and initiation of OMT in order to reduce their high pre-treatment mortality risk.
Financial Support: No external financial support.

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SEX, AGE, AND SYMPTOM-ASSOCIATED CHANGES IN BRAIN METABOLITES OF YOUNG MARIJUANA USERS.

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Aims: Marijuana (MJ) use often begins during adolescence and precedes other illicit drug use. We aim to investigate the effects of MJ use on adolescent brain development on brain metabolites, cognitive and psychiatric measures.
Methods: 54 young MJ users (13-23 years old, 30 males) and 42 controls (CON: 13-23 years old, 22 males) were evaluated. Self-reported psychiatric symptoms were assesed with the Symptom CheckList90. Structural MRI and localized 1H-MRS were performed at 3T. Spectra were obtained in 5 regions [anterior cingulate cortex, frontal white matter, basal ganglia (BG), cerebellum (CB), and thalamus]; metabolite concentrations were determined with LCModel. Groups were compared using ANCOVA (covaried for age) and posthoc regression analysis.
Results: MJ users were 19±2 years old, began using at 14±2 years old, and smoked 2±4 g/day, 6±2 days/week, for 53±43 months. CON were 19±2 years old, and 24 never used MJ; 18 used <10 joints in their lifetime. Some participants used nicotine or alcohol, but none were alcohol dependent. While there were no main effects of MJ, some metabolites showed interactions between MJ, sex and age ($p<0.05$). BG choline [CHO] decreased with age ($r=-0.4$ $p=0.05$) and was associated with more phobia ($r=0.7$ $p=0.004$) and somatization ($r=0.6$ $p=0.03$) in MJ females, while myo-Inositol levels (MI) increased with age ($r=0.4$ $p=0.02$) in the MJ males. CB N-acetyl-aspartate [NAA] decreased with age ($r=-0.5$ $p=0.01$) in the MJ males and was lower with longer duration of MJ use ($r=-0.4$ $p=0.04$) and more inter-personal sensitivity ($r=-0.4$ $p=0.05$). Creatine in CB increased with age only in CON females ($r=-0.5$ $p=0.04$).
Conclusions: Regular MJ use may impact adolescent brain development. Altered MI and CHO may reflect response to injury or disruption of age-associated changes in myelination or cellularity. Since we did not observe any cognitive deficits, which are often detected in adult MJ users, these subtle metabolite changes and psychiatric symptoms may precede cognitive deficits. Longitudinal follow-up of these subjects is ongoing.
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INDIVIDUAL DIFFERENCES IN REGIONAL BRAIN ACTIVATION DURING A TASK INVOLVING POTENTIAL MONETARY LOSS OR GAIN ARE ASSOCIATED WITH STRIATAL DOPAMINE RESPONSES TO AMPHETAMINE.

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Aims: PET and fMRI are increasingly used to study neurobiological risks for drug abuse, but links between the two bodies of research are ambiguous. This pilot study was conducted to test the hypothesis that brain activation during tasks involving monetary reward/loss (fMRI) is associated with dopamine responses to amphetamine (PET).
Methods: Five healthy subjects who completed [11C]raclopride PET scans in a study examining relationships among amphetamine (AMPH)-induced dopamine release (DAR), impulsivity, and stress were enrolled in a pilot study in which they completed a visual discrimination task while being scanned in a 3Tesla Philips Intera magnet scanner. The task included two different types of trials. In positively cued trials subjects expected to gain money for correct responses and to be treated neutrally for incorrect responses. In negatively cued trials they expected to lose money for incorrect responses and to be treated neutrally for correct responses. Activation was assessed in six brain regions selected a priori for their established roles in reward.
Results: BOLD responses in trials involving potential loss (threat) were more strongly associated with AMPH-induced DAR than responses in trials involving potential reward. Greater threat associated activation in the anterior cingulate, insula, and ventral striatum (VS) was linked to lower DAR in one or more striatal subdivisions (all $p \leq .05$). In contrast, more robust orbital frontal cortex activation in either threat ($p < .10$) or reward ($p < .05$) trials was associated with greater striatal DAR. Higher VS and hippocampal activation during reward trials was associated with more positive subjective drug effects (all < .10).
Conclusions: Findings suggest that risks for drug abuse may be influenced by exaggerated sensitivity to either negative or positive life events, but mechanisms are complex. The current methodology may be useful for elucidating critical underpinnings of such risks.
Financial Support: None.

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EVALUATING THE ACUTE EFFECTS PRODUCED BY SMOKING CAFFEINATED TOBACCO IN A WATERPIPE.

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Aims: Waterpipe (WP) tobacco smoking is a popular tobacco use method worldwide. Like cigarette smokers, many WP users report caffeine use while smoking. However, WP users also have the opportunity to smoke products that combine tobacco and caffeine (Tangiers F-Line). Anecdotal reports suggest that smoking the combined product produces greater effects than smoking tobacco without caffeine. These reports, coupled with novel smokeless caffeinated tobacco products (Revved Up), suggest a need to understand better the effects of these caffeinated tobacco products.
Methods: To address this need, a within-subjects study is ongoing in which participants smoke a WP (double-blind) for 45 min on four occasions that differ by product: caffeinated tobacco (CAFF/NIC), low nicotine caffeinated tobacco (CAFF), tobacco (NIC), or a nicotine-free caffeine-free product (PLACEBO). Outcome measures include plasma nicotine and caffeine, heart rate (HR), and subjectives. Twenty participants who report WP use (mean=8.8 WPs/month, SD=5.8) and daily caffeine use (mean=293.5 mg/day) have completed (40 completers are expected).
Results: Blood plasma is being assayed now to determine nicotine and caffeine concentration. Physiological data indicate significant HR increases occurred relative to baseline during CAFF/NIC and NIC but not during CAFF or PLACEBO. Subjective ratings of "good drug effects" and "like drug effects" increased significantly during all conditions, and the highest ratings were observed during CAFF/NIC and NIC. A significant increase in "lightheaded" was observed only during CAFF/NIC.
Conclusions: Preliminary analyses of physiological and subjective data suggest that effects are independent of caffeine content. Plasma data will reveal the extent to which using the combined product exposes the user to caffeine. Together, these outcomes will provide a more complete profile of the acute effects of smoking caffeinated WP tobacco and can be used to address the abuse liability of caffeinated tobacco products.
Financial Support: R01CA120142, R01DA024876, T32DA007027, and F31DA028102.

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SPONTANEOUS WITHDRAWAL IN OPIATE-DEPENDENT FISCHER 344, LEWIS AND SPRAGUE-DAWLEY RATS.

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Aims: The LEW and F344 inbred rat strains react differentially to acute morphine for a variety of behavioral and neurochemical measures. Investigations into effects of chronic morphine are less common than those assessing reactivity to acute treatment. With respect to these strains, studies assessing dependence have been limited to those utilizing antagonist-precipitated withdrawal. The present experiment extended these assessments by examining spontaneous withdrawal from morphine.
Methods: Males of the LEW, F344 and the outbred Sprague-Dawley strain were made dependent on morphine. Doses started at 10 mg/kg and were escalated to 100 mg/kg over the course of 15 days. Following this treatment, opiate administration was terminated and animals were examined for spontaneous withdrawal by the acquisition of a withdrawal-associated taste aversion, changes in body weight and the display of several behaviors characteristic of opiate withdrawal.
Results: Although all morphine-treated subjects decreased body weight and avoided consumption of the withdrawal-associated solution, indicating successful induction of dependence, no difference between the strains emerged in these indices of withdrawal severity. The only strain difference to appear in the behavioral indicators of withdrawal was with diarrhea (LEW > F344).
Conclusions: That the LEW and F344 strains displayed a behavioral profile reflective of opiate withdrawal, but displayed no differences, is surprising given the reported differential responsivity of these strains with respect to acute opiate administration. Although the spontaneous withdrawal preparation is more similar to the human condition relative to withdrawal from opiates, it is not commonly utilized in animal models of dependence and withdrawal due to the effects being less pronounced and harder to detect. An examination of changes in overall opioid tone in discrete brain areas after chronic opiate exposure in these strains would provide more insight into the possible mechanisms for reported genotypic differences in drug self-administration.
Financial Support: Supported by a grant from the Mellon Foundation to ALR.

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MISSED OPPORTUNITIES FOR HEPATITIS C VIRUS SCREENING IN COMMUNITY-BASED DRUG TREATMENT CENTERS.

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Aims: Hepatitis C Virus (HCV) infection is a significant public health problem frequently associated with injection drug use (IDU), though many IDUs have never been screened for HCV. We identified characteristics associated with HCV testing among IDU attending community based drug treatment programs.
Methods: We collected HCV testing history from 1281 participants in a randomized controlled trial of HIV counseling and testing strategies in community based drug treatment programs. We assessed characteristics associated with HCV testing among the 622 participants with a history of IDU using logistic regression and examined whether there was an association between self-reported HCV testing history and specific risk behaviors using contingency table methods.
Results: 36.7% of 622 IDU had never been tested for HCV. Men were less likely to have ever been tested than women (OR 0.60; CI 0.40, 0.92), as were Blacks vs. Whites (OR 0.54; CI 0.30, 0.98). IDU with a history of incarceration (OR 2.30; CI 1.37-3.84), and those attending a medication assisted treatment program (OR 2.17; CI 1.26-3.74) were more likely to report having been tested for HCV, while those without prior HIV testing were less likely to have been tested for HCV (OR 0.30; CI 0.20-0.46). IDU who had previously tested HCV-positive were less likely to report problem alcohol use (HCV-positive 129/235=54.9%, HCV-negative 104/159=65.4%, HCV status unknown 167/228=73.3%, p<.001).
Conclusions: Many IDU in drug treatment programs had never been tested for HCV. Renewed efforts to integrate HCV screening into drug treatment programs and other high-risk settings are needed.
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TOBACCO USE PATTERNS AMONG ADOLESCENTS ENTERING SUBSTANCE ABUSE TREATMENT.

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Aims: The aims of this study are to explore tobacco use patterns among adolescents who are entering substance abuse treatment and compare these to use patterns at 90 days post-intake (i.e., follow-up), examining any gender differences that exist in these patterns.
Methods: Data are from 143 substance abuse treatment facilities across the United States that administer the Global Appraisal of Individual Needs (GAIN). All data were collected as part of general clinical practice under their respective voluntary consent procedures and were subsequently de-identified. The pooled data were gathered from GAIN interviews with 14,332 adolescents (ages 12-17), of whom 3,875 are female.
Results: Approximately 47% (n=6,666) of adolescents acknowledged weekly tobacco use at intake. Among these, 71.2% were tobacco-dependent or used tobacco daily. Females more frequently reported dependence/daily use (76.6% vs. 69.0% for males; $\chi 2(3)=41.2$, p<.001), high levels of past-year dependence (8.7% vs. 4.3%; $\chi 2(3)=79.7$, p<.001), and that tobacco caused past-month problems (12.6% vs. 7.7%; $\chi 2(3)=32.6$, p<.001). Females reported smoking more days out of the past 90 at intake (70.1 vs. 66.7 for males; $F(1,6664)=22.1$, p<.001), but the same number as males at follow-up (37.1 vs. 36.5; n.s.). Conversely, males smoked more times per day at intake (8.1 vs. 7.6 for females; $F(1,6624)=4.9$, p<.05), but smoked the same number of times per day at follow-up (7.3 vs. 6.8; n.s.). At follow-up, all adolescents smoked less often and fewer times per day than at intake.
Conclusions: Given the number of adolescents entering substance abuse treatment with weekly tobacco use, it is important for substance abuse treatment to address tobacco use as a component of treatment. Interventions should be tailored to adolescents, with specific emphasis on females who may be smoking more often than males and experiencing more significant dependence symptoms.
Financial Support: The development of this poster was supported by the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment under contracts 207-98-7047, 277-00-6500, 270-03-00006, and 270-2007-00004C using data provided by grantees.

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PUBERTAL STATUS AS A PREDICTOR OF INCREASED RISK-TAKING ON A LABORATORY TASK.

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Aims: Adolescence is a developmental period marked by the emergence and escalation of risk taking, including substance use initiation and progression. A proposed explanation for the escalation in risk behavior engagement is pubertal onset, defined as the child's degree of physical and sexual maturation, which has been associated with increased risk taking, beyond the effects of age. To understand the effect of pubertal status in adolescent risk taking, the current study investigated this relationship using a behavioral analogue task.
Methods: The sample consisted of 244 adolescents (44% girls), 9-13 years old (mean age = 13.05 +/- .896; 49% White; 35% Black). Participants self-reported their pubertal status using the Pubertal Developmental Scale by rating physical changes caused by puberty. The scores range from 1 (have not begun) to 4 (completed). The mean pubertal score for girls was 2.43 and for boys 2.30. Risk taking was measured using the Balloon Analogue Risk Task (BART), a behavioral measure of risk-taking propensity.
Results: Participants were categorized according to their pubertal status: low puberty (absent to minimal development) and high puberty(moderate to full development). The high puberty group evidenced higher risk taking on the BART than the low puberty group, but only for girls (p=.017). Findings were sustained when examining puberty continuously.
Conclusions: Results indicated a greater propensity to take risks among girls with moderate to full pubertal development compared to those with no to minimal development, a finding supported by self report but not established with behavioral measurement. Due to the cross-sectional nature of the study, we are unable to determine if the effect is due to early pubertal timing or the presence of puberty. Nevertheless, results indicate a promising link for girls between puberty and risk taking with an objective measurement in a controlled laboratory setting. This suggests the importance of isolating the role of puberty or examining early pubertal timing specifically, to determine their effect on risk-taking.
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REPEATED ADMINISTRATION OF A MUTANT COCAINE ESTERASE: EFFECTS ON PLASMA COCAINE LEVELS, COCAINE-INDUCED CARDIOVASCULAR ACTIVITY, AND IMMUNE RESPONSES IN RHESUS MONKEYS.

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Aims: These studies were aimed at 1) characterizing the immunologic responses to repeated dosing with a mutant cocaine (COC) esterase (T172R/G173Q; DM CocE), and 2) determining if the development of anti-CocE antibodies alters the capacity of DM CocE to reduce plasma COC levels and ameliorate the cardiovascular effects of COC in rhesus monkeys.
Methods: Each monkey (n=5) completed a total of five trials. Administration 3 mg/kg;IV COC followed 10 min later by PBS served as the baseline condition, with 0.32mg/kg;IV DM CocE administered 10 min after 3 mg/kg;IV COC during four, bi-weekly trials. Three monkeys, implanted with telemetric probes (DSI; D70-PCT), were used to evaluate the effects of DM CocE on COC-induced changes in BP and HR, and two rhesus monkeys were used to evaluate the effects of DM CocE on plasma COC levels, with plasma samples were collected immediately before, and 8, 15, 30, 60, 90, and 120 min after COC administration. Serum samples for anti-CocE antibody titer determinations were collected 24h before test sessions.
Results: During baseline conditions, COC exhibited an elimination half-life of approximately 45 min, and resulted in persistent increases in BP and HR. Administration of DM CocE resulted in a rapid elimination of COC, with plasma levels below detectable limits within 5-8 min of DM CocE. A similarly rapid amelioration of COC-induced increases in BP and HR was also observed, with baseline-like measures generally observed within 20 min of DM CocE. Although slight (10-fold) increases in anti-CocE antibodies were observed following the fourth test, these antibodies did not alter the capacity of DM CocE to reduce COC plasma levels, or reverse the COC-induced increases in BP and HR. Titers generally dissipated within seven weeks.
Conclusions: Together, these results suggest that DM CocE may provide a novel and effective therapeutic for the treatment of acute COC toxicity.
Financial Support: NIDA grant DA023213

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MARIJUANA PURCHASING BEHAVIOR AMONG YOUNG-ADULT MARIJUANA USERS.

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Aims: Marijuana (MJ) users' purchasing behavior has not been widely studied. Indeed, the price elasticity of MJ is unknown. Behavioral economics (BE) approaches suggest that drugs are similar to other commodities in their relation to constructs such as price elasticity (e.g., increases in price lead to reductions in MJ use) and relative reinforcement value (RRE). The aim of this study was to examine features of MJ users' purchasing behavior as part of a BE study. We tested this aim using a sample of young-adults (age 18-30 years) who were regular (i.e., > 3x/week) MJ users.
Methods: The sample (n = 28) was 57% male. Participants completed an interview about their typical MJ use and MJ purchases and a simulated MJ-purchasing task to assess the RRE of MJ. For the simulation task, they imagined that they had 4 hours to be alone smoking high-grade MJ. They were asked how many average-sized MJ joints they would smoke, if the price for a joint was __X__; the X price ranged from $0 to $160/joint.
Results: Our preliminary data are based on interviews of the sample to date (n = 28) from an ongoing study (N = 50). Young adults purchased MJ several times/week (n = 9) or month (n = 13); mode = once/week. Most purchased about 7 joints (range = 1 to 56), spending $40 (SD = $24) on a typical MJ purchase. They estimated spending about $175/ month on MJ (range = $40-$600; SD = $151; Mdn = $110). MJ was purchased from a friend (n = 19), strangers (n = 4) or a family member (n = 4). Most (n = 20) did not trade goods or services for MJ. Data from the simulation task will be used to generate five RRE measures (e.g., breakpoint, intensity of demand).
Conclusions: Young-adult MJ users purchase high quantities of MJ, on which they spend a lot of money. To the extent that we apply BE approaches to understanding the economic parameters of MJ use, we may be able to use BE-based strategies in the development of effective secondary-prevention strategies for MJ use.
Financial Support: R01 DA027606 from NIDA/NIH to R.L. Collins (PI).

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KNOWLEDGE ABOUT LEGAL BLOOD ALCOHOL CONTENT LIMITS FOR DRUNK DRIVING IN A SAMPLE OF BRAZILIAN DRIVERS.

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Aims: In Brazil the legal blood alcohol content (BAC) allowed for driving was changed to zero in 2008. If the BAC found is above 0.06 mg/dl, drivers may be arrested. However, there are limited data on drivers'knowledge about such limits. The aim of this study was to verify drivers'knowlegde about legal BAC limits.
Methods: Drivers from 27 major metropolitan areas(n=3,397)were randomly asked to participate in roadside survey from 12 a.m. to 12 p.m. on Fridays and Saturdays. They were breathalized by highway patrol officers, and after consent interviewers collected data on drinking behaviors, knowledge about the law, and breath tests results.
Results: The mean age was 37.3± 11.3 years ; 94.3% were male and 27.8% had at least started high school. When asked about the BAC that could result in prison, 34.5% of the subjects claimed to know it. However, only 23.5% (8.1% of the total sample) provided correct answers. Factors associated with the right answers were: male gender (p=0.04; OR= 2.08; IC= 1.01-4.27); higher education (p<0.0001); negative BAC or self-report of DUI (p=0.041); higher family income (p=0.01) and non-professional driving (p=0.041). Age was not statistically different between groups. After multivariate analysis, male gender (p=0,002), higher education (p<0,0001) and negative BAC or DUI (p=0,046) remained in the model.
Conclusions: The knowledge that BAC levels over 0.06mg/dl can result in inprisonment is sparse among Brazilian drivers, notably among women, the less educated and those who drink and drive . Educational programs targeted at those specific groups may be necessary in order to increase awareness about the legal BAC limit and its consequences.
Financial Support: Brazilian Secretariat for Drug Policies

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TREATMENT WITH A GLIAL MODULATOR ATTENUATES OPIOID TOLERANCE AND DEPENDENCE IN OPIOID-DEPENDENT VOLUNTEERS.

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Aims: Preclinical studies demonstrate that glial cell activation contributes to opioid tolerance and dependence.This study examined the effects of the glial cell modulator ibudilast on opioid tolerance and dependence in dependent volunteers.
Methods: For this 21-day, double-blind, within- and between-subject study, heroin-dependent volunteers (N=29) were maintained on morphine (30 mg,QID) for 2 wks and placebo (QID) on the 3rd wk. On Day 8, participants were randomized to receive placebo (P;0mg BID), low (L;20mg BID), or high dose (H;40mg BID) ibudilast. To assess effects of ibudilast on tolerance, oxycodone's (O;0,25 & 50mg) analgesic, subjective, and physiological effects were measured before and after randomization (Days 4&11). To assess analgesia, participants immersed a hand in cold water, and times to report pain and withdraw the hand from the water were recorded. Subjective pain ratings were measured, as were subjective ratings of drug effect and miosis (M).
Results: Subjective opioid withdrawal ratings were higher during the 3rd wk relative to 1st & 2nd wks in P & L groups, but not in the H group. O's analgesic effects were blunted in the P group during the 2nd wk relative to the 1st, whereas O-induced decreases in subjective pain ratings were lower during the 2nd relative to the 1st wk in the H group. Similarly, tolerance was observed to the physiological effects of O in the P group with decreased O-induced M during the 2nd wk, whereas increased O-induced M in the L & H groups was observed during the 2nd wk.The H group also reported higher O-induced positive subjective drug effects during the 2nd wk relative to the 1st wk.
Conclusions: Under the current conditions ibudilast decreased the subjective symptoms of withdrawal and seemed to prevent, and in some cases reverse, tolerance to opioid-elicited analgesic, physiological, and subjective effects. These findings are the first to demonstrate the potential clinical utility of glial modulators for opioid dependence in humans.
Financial Support: Supported by DA09236-15

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A PILOT STUDY OF POSTAL TREATMENT FOR CANNABIS DEPENDENCE.

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Aims: In Australia, many would-be treatment seekers for problematic cannabis use live in rural and remote areas, thereby decreasing their access to treatments that are face-to-face. In order to address this gap in treatment availability, the present study aimed to assess the feasibility of a mail-based treatment for dependent cannabis users.
Methods: Using a single group pre/post design, this study compared cannabis use at baseline, post-treatment, and a 1 month follow-up. Treatment was based upon cognitive-behavioural and motivational interviewing principles, and consisted of six treatment modules posted fortnightly to participants. In addition, participants received personalised feedback at four points during the treatment, based upon their mailed-in responses to the modules. Participants were recruited through advertisements in rural newspapers and through a Google advertisement. Friedman's Analysis of Variance (ANOVA) was used to compare cannabis use at baseline and at post-treatment and follow-up.
Results: A total of 86 people completed baseline assessments in this study and 34 participants went on to complete treatment. Overall, treatment completers significantly decreased ($\chi 2=40.82$, $p<0.001$) their cannabis use over the course of this study. Baseline observation carried forward for missing data also demonstrated a significant reduction in cannabis use ($\chi 2=35.93$, $p<0.001$). Furthermore, of the 34 who completed treatment, nearly one quarter (n=8) were abstinent at follow-up.
Conclusions: Transposing face-to-face treatments into a postal format has shown some promise and future research is warranted to determine the efficacy of such treatments in a controlled study.
Financial Support: This project was funded by the Australian Government Department of Health and Ageing

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NEUROCOGNITIVE FUNCTIONING AMONG PATIENTS RECEIVING TREATMENT FOR SUBSTANCE USE DISORDERS: SOCIODEMOGRAPHIC AND DRUG USE CHARACTERISTICS.

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Aims: The purpose of this study was to examine the sociodemographic and drug use characteristics associated with cognitive impairment in patients with substance use disorders (SUD).
Methods: Neuropsychological functioning was examined in 60 partial hospital and intensive outpatients using the Neuropsychological Assessment Battery (NAB). Standard scores were calculated based on demographically corrected test norms relative to a standardization sample of neurologically healthy individuals of the same age, sex, and educational level.
Results: Men (n=31) performed better (M=103.3, SD=14.0) than women (n=29; M=94.3, SD=17.1) on visuospatial measures ($p < .05$). Among women, days of amphetamine use in past year was associated with poorer attention; days of benzodiazepine use in the past 90 days and in the past year was associated with poorer visuospatial performance (p's < .01). Among men, days of alcohol use in past 90 days and past year, and days of amphetamine use in past 90 days, were associated with poorer visuospatial performance; days of opioid use in past 30 and 90 days was associated with poorer language performance (p's < .05). Age was split based on its bi-modal distribution. Patients < 35 years of age (n=25) performed better (M=118.4, SD=18.2) than persons > 35 years of age (n=35) (M=98.7, SD=10.5) on measures of language processing. Among patients > 35 years of age, days of cannabis use in past 30 and 90 days was associated with poorer executive function and language performance (p's < .05); days of cocaine use in past year was associated with poorer executive function; and days of amphetamine use in past year was associated with poorer visuospatial performance (p's < .05).
Conclusions: These findings highlight important gender- and age-related differences that may suggest the need for differential cognitive rehabilitation or accommodation approaches adjunctive to SUD treatment.
Financial Support: Supported by NIH grant 1R03DA024126 (Copersino), 1K23DA027045 (Copersino), 5K24DA022288 (Weiss)

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UNEXPECTED CHANGES IN STRIATAL ACTIVATION WITH TREATMENT DURING THE GUESS/REWARD FMRI TASK IN COMORBID MDD-CUD YOUTH.

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Aims: Preference for immediate over delayed rewards is associated with impulsivity, and is a risk factor for addictive disorders. Reward behavior has been shown to be mediated by the ventral striatum. The aim of this study was to assess activity for reward as shown by fMRI neuroimaging before and after treatment among older adolescents and young adults with comorbid cannabis dependence/major depression. Non-comorbid depressed patients typically show an increase in activity for reward as their depression decreases with treatment.
Methods: Five subjects were recruited from a NIDA-funded treatment study. Each of those subjects completed the guess/reward task (developed by Delgado and Fiez) during a BOLD fMRI scan both before and after a 12-week treatment study.
Results: The expected activation was noted in the insula, prefrontal, and striatal areas, both before and after treatment. However, the participants showed lower activity for reward after treatment rather than before treatment, which is opposite of what would be expected in depressed subjects who did not demonstrate a comorbid substance use disorder.
Conclusions: These unexpected findings suggest that the potential increase in activity for reward associated with treatment for depression may have been overshadowed the decrease in activity for reward associate with treatment of pathological cannabis use in these comorbid subjects. Our current findings are analogous to recent findings involving the fMRI "faces" task (Cornelius, Hariri, & Aizenstein, 2010), in which findings involving a comorbid MDD/SUD population were substantially different from those involving non-comorbid subjects.
Financial Support: NIDA grants R01DA019142, R01DA019142-04S1, K02DA017822, P50DA05605; NIAAA grants R01AA15173, R01AA013370, K24AA015320, and K02AA00291.

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DETERMINING EFFICACIOUS DOSES OF METYRAPONE AND OXAZEPAM COMBINATIONS TO TREAT METHAMPHETAMINE CUE-REACTIVITY IN RATS.

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Aims: We have previously reported that the combination of low doses of metyrapone (MET), a corticosterone synthesis inhibitor, and oxazepam (OX), a benzodiazepine receptor agonist, reduces intravenous cocaine self-administration and the cue-induced reinstatement of extinguished cocaine seeking in rats. This experiment was designed to explore various individual and combination doses of MET and OX for treatment of methamphetamine (METH) cue-reactivity.
Methods: Adult male rats were implanted with jugular catheters and trained to self-administer METH (0.06 mg/kg/infusion) during daily 2-h sessions. During training, METH delivery was paired with the presentation of a tone and the illumination of a houselight. Once stable baselines of self-administration were observed, rats were placed into forced abstinence, where they remained in their home cages for 14 days. During cue reactivity testing on the 15th day, the rats were placed in the operant chambers and responding only resulted in the presentation of the conditioned reinforcer (i.e., the houselight and tone previously paired with METH delivery during self-administration); no METH was delivered. The response-contingent presentation of the conditioned reinforcer reliably maintained METH seeking (i.e., lever pressing) following vehicle pretreatment.
Results: Pretreatment with OX (2.5, 5, and 10 mg/kg) dose-dependently attenuated cue-reactivity responding. Pretreatment with MET (25, 50, 75 and 100 mg/kg) attenuated responding at the highest dose tested. Pretreatment with combinations of 25 mg/kg MET/5mg/kg OX or 50 mg/kg MET/10mg/kg OX resulted in dose-dependent attenuation of meth seeking.
Conclusions: These data suggest that the combination of MET and OX may be useful in treating the relapse to methamphetamine use.
Financial Support: This project was funded by the department of Pharmacology, Toxicology and Neuroscience at the Louisiana State University Health Sciences Center in Shreveport, Louisiana.

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HIV RISK AND TREATMENT AMONG OPIATE INJECTORS.

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Aims: This study examines two interventions for opiate-using injection drug users (IDUs). The two interventions are strengths-based case management (CM) vs. strengths-based case management plus a facilitated therapeutic alliance (CM/FTA). In the FTA, case managers facilitate a relationship between treatment counselors and clients. Outcomes include methadone treatment engagement and retention, and reduction of HIV risk.
Methods: Four hundred and ten IDUs were recruited through street outreach in Denver from 2007-2010. Subjects were randomly assigned to receive either CM (n=205) or CM/FTA (n=205) intervention. There were no significant demographic or HIV risk differences at baseline between the participants assigned to CM vs. CM/FTA. Participants were 54% white, 74% male and averaged 41 years old. Two hundred and thirty-seven participants were followed at 6 months.
Results: Participants in the CM/FTA condition were significantly more likely to stay in treatment for more than 90 days than those in CM (74% vs. 48%, p=0.02). Treatment entry was associated with significantly more reduction in injection drug use in the 30 days prior to 6-month follow up (p<0.0001). When looking at baseline differences in treatment entry, those who entered treatment reported more heroin (p=0.001) and drug use (p=0.04) and were more likely to be employed (p<0.0001). For those who stayed in treatment for more than 90 days, they were significantly more likely to report a reduction in injection drug use (p=0.047) and HIV risk behavior (p=0.045) at 6-month follow up than those who left treatment before 90 days. This trend remained for women when analyzed separately. Finally, multiple logistic regression revealed that being employed (p=0.0001), injecting more heroin (p<0.0006) and not having sex with an IDU (p=0.045) at baseline predicted treatment entry.
Conclusions: Evidence was found for the effectiveness of adding the FTA to CM for treatment retention. This study also shows the benefit of treatment entry and retention on HIV risk behaviors and drug use.
Financial Support: This study was supported by the National Institute on Drug Abuse, DA09832.

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ANKK1 POLYMORPHISMS MAY INFLUENCE BETA2-NICOTINIC ACETYLCHOLINE RECEPTOR AVAILABILITY IN NONSMOKERS.

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Aims: Genetic differences influence susceptibility to nicotine dependence and may impact treatment response. The most prevalent nicotinic acetylcholine receptors (nAChRs) in the brain contain alpha4 and beta2 subunits and demonstrate high affinity for nicotine as well as the nicotinic agonist radiotracer [123I]5-IA-85380 (5IA). In this study, we evaluated the relationship between single nucleotide polymorphisms (SNPs) at two genes that have been associated with nicotine dependence (CHRNA4 and ANKK1) with beta2-nAChR availability in nonsmokers.
Methods: To date, 40 healthy European-American nonsmokers (aged 32+13, 21 women, 19 men) have been imaged with 5IA SPECT and genotyped. 5IA was administered as a bolus plus constant infusion and subjects were scanned at equilibrium (6-8 hrs post-injection). An MRI was obtained to guide the placement of the regions of interest: thalamus, striatum, cerebellum and cortical regions. SNPs were genotyped via Taqman. ANOVAs were conducted with Bonferroni as the post-hoc.
Results: In preliminary analyses, for the CHRNA4 SNPs (rs2273502, rs2273504, rs2236196), there were no significant differences across genotypes on beta2-nAChR availability. For the ANKK1 SNP (rs4938013), there were significant differences in beta2-nAChR availability ranging from 23-46% in the thalamus, striatum and cortex (p<0.05)
Conclusions: Our preliminary results suggest SNPs at the ANKK1 gene locus may modulate beta2-nAChR availability in nonsmokers, providing a straightforward biological rationale to previously reported statistical associations. The ANKK1 gene encodes a tyrosine kinase, and thus may phosphorylate the nAChR in a manner that alters nicotinic agonist binding.
Financial Support: This research was supported in part by National Institute of Health grants RO1 DA015577 and KO1 DA20651.

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PILL RECOGNITION AND PRESCRIPTION STIMULANT BRAND NAME IDENTIFICATION IN N-MAPSS.

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Aims: Stimulant abuse by young people is of concern because the availability of these drugs for the treatment of ADHD has risen 80% in the last decade (Setlik et al, 2009). SAMHSA's Office of Applied Statistics estimates of past month illicit use of stimulants among 12 to 17 year olds have been 0.5% to 0.9% over the last decade. Although findings come from teens' self-report, no data are published on stimulant pill recognition among youth. This analysis assesses the extent to which 10 to 18 year olds are able to correctly identify specific prescription stimulants.
Methods: Youth 10 to 18 years of age (N=5,423) were recruited via an entertainment venue intercept method in 10 metropolitan areas throughout the U.S. for the National Monitoring of Adolescent Prescription Stimulants Study (N-MAPSS). The youth filled out an anonymous survey that included pictures of 5 different dosages of the most commonly prescribed amphetamine salt (AS). Youth were asked: "Have you ever seen this medicine?" Those that said "Yes" were asked to name it. Responses were coded as: All correct; Correct name but dose/release incorrect; Correct name but not otherwise specified (NOS); or Incorrect. Phonetically correct misspellings were accepted as correct.
Results: 20% of 10-12 year olds (n=738), 19% of 13-15 year olds (n=2,171) and 27% of 16-18 year olds (n=2,514) said they had seen at least one of the 5 images of the AS; however only 3%, 6% and 15% respectively, correctly identified it. Of 261 current AS users, 82% reported seeing the drug and 69% correctly named it; compared to 20% and 7% of non-users (n=5,148). The 2 images of extended release capsules were more often correctly named (68%) than the immediate release tablets (13%-20%). Almost all correct identifications were of the NOS type.
Conclusions: While 20% of youth report seeing an AS, only 3% to 15% could correctly identify it. The highest rates of correct identification were among youth who reported recent use of AS. More work is needed to understand what youth know about AS and other prescription stimulants.
Financial Support: Contract through Pinney Associates with funding from Shire Pharmaceuticals.

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ADDICT'PREV : A MOTIVATIONAL WEBSITE DEDICATED TO DRUG USE AND ABUSE PREVENTION FOR STUDENTS IN A FRENCH AREA.

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Aims: Drug use and abuse are major problems of public health especially in the students' population (where binge drinking e.g. is occuring recently widely). As this population has poor interest to meet health services and more to use Information and Communication Technologies, we decided to develop a website dedicated to those problems'evaluation and prevention.
Methods: The University Health and Prevention Service has developed an original tool to reach a 32,000 students' potential target in the Clermont Ferrand area. This website (www.addictprev.fr) provides three services. First of all is an information about psychoactive drugs including alcohol and tobacco. The second one is a list of links including other websites (mostly national) regarding addiction prevention but also useful addresses (e.g. where to ask for care ?). Last but not least, the site propose self evaluation of one's consumption and well being through six questionnaires. Three are for alcohol (AUDIT), tobacco (Fagerstrom) and cannabis (CRAFFT inspired questionnaire). It also offers three additional questionnaires. One is about the psychological status (GHQ), another is about quality of life (SF36). The final one is related to a printed document we'd developed about alcohol : What do ? What to say ? The site has opened on january 2010.
Results: Intermediate qualitative evaluation has been realized in june 2010 with semi-directive interviews in 22 students . We'll present those results as well as quantitative about the first year functioning (including number of connections, most frequent days, etc.)
Conclusions: According to the first results this tool could be shared with other UHPC especially those we had presented in the LARA 2 survey (Courty P, CPDD 2010) but also extended to all students health services in France.
Financial Support: Supported by MILDT (French inter ministerial drug prevention office)

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CRAVING AND SEVERITY OF CANNABIS DEPENDENCE MODULATE BRAIN RESPONSES TO CANNABIS CUES.

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Aims: The main goal of the current functional Magnetic Resonance Imaging study was to investigate neural correlates of visual cannabis cues in relation to levels of cannabis use and problematic cannabis use.
Methods: Cue-induced brain activity was compared between heavy cannabis users(n = 31), sporadic cannabis users (n = 20), and cannabis naive healthy controls(n = 22) . Within heavy cannabis users, a subgroup with a high level of problematic cannabis use was compared to a subgroup with a low level of problematic cannabis use and relations between cue-induced brain activity, craving, frequency of cannabis use, and duration of cannabis use were explored.
Results: Viewing cannabis versus control images in heavy users compared to sporadic users and controls was associated with activity in the orbitofrontal cortex and ventral tegmental area . Within heavy users, high- compared to low-dependent individuals showed differences in the nucleus accumbens, caudate, orbitofrontal cortex, thalamus, insula, hippocampus. Activity in the left dorsolateral prefrontal cortex and pre-motor area correlated negatively with subjective craving in heavy users.
Conclusions: This is the first study demonstrating that cannabis cues activate areas associated with addiction pathology in heavy cannabis users compared to sporadic users and controls. Within heavy cannabis users, craving and severity of dependence, but not cannabis use history modulated cue-reactivity, indicating that symptoms of dependence, rather than the amount of cannabis use, plays an important role in cue-reactivity. These findings support a role of cue-reactivity as a biomarker in the diagnosis and prediction of cannabis dependence.
Financial Support: Supplement to NIDA grant DecisionMaking in Marijuansers R01 DA022274 awarded to A.E. Goudriaan, D.J. Veltman, and W. van den Brink.

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12-MONTH OUTCOMES OF A PILOT STUDY OF EXTENDED-RELEASE INJECTABLE NALTREXONE FOR OPIOID-DEPENDENT PROBATIONERS AND PAROLEES.

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Aims: Opioid-dependent community corrections clients have high relapse and recidivism rates. The aim of this open label trial was to examine 12-month outcomes among opioid-dependent probationers and parolees who were treated with extended release injectable naltrexone (XR-NTX).
Methods: A total of 39 opioid-dependent adults who were under community supervision for at least six months were recruited from Philadelphia, PA and Baltimore, MD. All participants received up to six monthly injections of Depotrex® brand XR-NTX and 28 (72%) were re-assessed six months after their last injection (i.e., 12-months post–treatment entry). Outcome measures included urine drug screens for opioid use, incarcerations and employment. The analysis compared those who received all six planned injections (n=17; 61% completers) to those who did not (n=11; 39% non-completers).
Results: The sample was predominately male (90%) with an average age of 37 years; 62% were Caucasian, one-third were African-American and 5% were Hispanic. The 12-month findings demonstrate that the completer group as compared to the non-completer group had lower incarceration rates (6% vs. 46%;p=.013) and were more likely to be working (71% vs. 20%;p=.011). While the proportion of opioid positive urine tests were lower among treatment completers than non-completers (25% vs. 57%), the difference was not significant.
Conclusions: Extended release naltrexone may be a promising treatment for opioid dependent probationers and parolees to prevent relapse and criminal recidivism. An ongoing multi-site randomized trial is currently in the field to further assess the effectiveness of XR-NTX for this population.
Financial Support: NIDA grant R01DA012268 and Dana Foundation.

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5-HT2C RECEPTOR ACTIVATION ATTENUATES COCAINE-INDUCED CONDITIONED PLACE PREFERENCE AND HYPERACTIVITY.

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Aims: Previous studies have identified an inhibitory regulatory role of the 5-HT2C receptor in dopamine neurotransmission. Activation of 5-HT2C receptors has been shown to decrease cocaine-induced dopamine release in mesolimbic brain areas associated with reward circuitry. Administration of 5-HT2C receptor agonists prior to cocaine administration elicits an attenuation of cocaine-induced behaviors such as hyperactivity and cocaine self-administration. In this study, the role of 5-HT2C receptors in cocaine-induced, dopamine-mediated behaviors was investigated using the conditioned place preference paradigm, in which the development of conditioned reward-seeking behavior as well as acute cocaine-evoked hyperactivity was assessed.
Methods: Alterations in the development of cocaine-seeking behavior were assessed using a biased design of the CPP model, in which C57/Bl6 male mice (n=8-12/group) were treated with a 5-HT2C receptor agonist, RO 60-0175 (1, 3, 10 mg/kg, i.p.), 30 minutes prior to cocaine administration (10 mg/kg, i.p.) on treatment days. Immediately following cocaine administration, mice were placed in the treatment-paired side of the testing chamber. On alternate days, mice were injected with saline (2 injections 30 minutes apart) and placed in the opposite side. Preference was tested in a drug-free state after 4 days of conditioning. Locomotor activity was assessed on each day while in the testing chambers.
Results: Mice treated with RO 60-0175 prior to cocaine administration exhibited a significant dose-dependent decrease in CPP behavior as compared to saline-pretreated controls. Likewise, administration of RO 60-0175 prior to cocaine exposure resulted in an attenuation of cocaine-induced hyperactivity as compared to saline-pretreated controls.
Conclusions: These data support a role for the 5-HT2C receptor in regulating cocaine-mediated behaviors, thus identifying a potential pharmacological therapeutic target for further investigation for preventing relapse and promoting abstinence in cocaine-dependent individuals.
Financial Support: DA09580 (E.M.U.)
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EARLY METHYLPHENIDATE TREATMENT DIFFERENTIALLY AFFECTS CONDITIONED AND UNCONDITIONED COCAINE ACTIVITY.

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Aims: A recent study in our laboratory found that methylphenidate (MPH) treatment during the preweanling period increased the reinforcing strength of cocaine (COC) as assessed by self-administration but had no effect on cocaine-induced conditioned place preference. These results suggested that early MPH treatment may enhance the unconditioned effects of cocaine but not the effects of COC-paired environmental cues. Thus, the goal of the current study was to further examine the effects of early MPH exposure on COC and COC-paired cues using a conditioned activity paradigm.
Methods: We treated rats with MPH (0, 2, or 5 mg/kg) from postnatal day (PD) 11 to PD 20. Beginning on PD 60, rats were given injections of COC (0, 15, or 30 mg/kg) and placed in activity chambers for seven consecutive days. Rats were then injected with saline and tested for conditioned activity three or ten days after the last cocaine injection. COC pre-exposure sessions lasted 60 min and test day sessions lasted for 120 min.
Results: Female rats were more active than males during both the COC pre-exposure phase and on the test days. MPH pretreatment (2 mg/kg) increased activity compared to vehicle- and MPH- (5 mg/kg) treated rats over the seven day COC pre-exposure phase. Exposure to cocaine (15 and 30 mg/kg) during the COC pre-exposure phase induced conditioned activity in all MPH groups on both test days. Female rats in the MPH (2 mg/kg) group had increased activity on test day 2 compared to the vehicle and MPH (5 mg/kg) group.
Conclusions: The present data suggest that early exposure to MPH may enhance the effect of COC-paired environmental cues but only in females.
Financial Support: R24DA025319

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LY379268, A SELECTIVE GROUP II METABOTROPIC GLUTAMATE RECEPTOR AGONIST, DOSE DEPENDENTLY DECREASES METHAMPHETAMINE SELF-ADMINISTRATION IN RATS.

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Aims: Given the significant problems associated with the current escalation in methamphetamine use, the identification of more effective treatment strategies is essential. Group II metabotropic glutamate receptors (mGluR2/3) have been suggested to be a potential novel therapeutic target for psychostimulant addiction. Indeed, selective agonists such as LY379268 have been shown to be effective in reducing the consumption of cocaine in pre-clinical animal models. No studies to date, however, have assessed the effects of mGluR2/3 agonists on methamphetamine consumption. The aims of this study were to evaluate the efficacy of LY379268 in reducing methamphetamine self-administration.
Methods: Adult, male Sprague-Dawley rats were implanted with chronic indwelling catheters in the right jugular vein and were trained to self-administer methamphetamine on a FR1 schedule (0.05 mg/kg per infusion, delivered over 2 seconds) during a two hour session. Rats were then pre-treated with vehicle or LY379268 (0.56, 1, or 3 mg/kg, i.p.) 30 minutes before a self-administration session. The effects of LY379268 on methamphetamine self-administration were then assessed. Stable responding back to baseline values was re-established in between drug treatment sessions.
Results: LY379268 dose-dependently reduced responding for methamphetamine, with virtually complete suppression after 3 mg/kg. Responding for methamphetamine was also significantly lower following 1 mg/kg (N=7). Though no significant effects on responding occurred with 0.56 mg/kg LY379268, there was a trend for a decrease (N=7).
Conclusions: These findings demonstrate that group II mGluRs play a significant role in the consumption of methamphetamine, and that selective agonists may reduce this behavior. Additional investigation with chronic administration of LY379268 is needed, however, to determine the utility of this compound as an effective pharmacotherapy for methamphetamine addiction.
Financial Support: This research was funded by the NIDA Grants DA14030 (DCSR) and DA26590 (TJRB).

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ON-GOING REAL TIME ANALYSIS OF DRUG USE, MENTAL HEALTH PROBLEMS AND HEALTH CARE UTILIZATION OF VETERANS VS. NON-VETERANS.

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Aims: We aim to compare mental health, drug use, and health care use between Veterans and non-Veterans in a community-recruited sample, hypothesizing that Veterans would have more need for services and less access to those services than non-Veterans.
Methods: HealthStreet, a community-based outreach and research hub for Washington University in St. Louis utilizes community health workers to address health issues, and to educate and recruit a diversified population for studies, as a part of the Institute for Clinical and Translational Sciences. The Health Intake Form recently added a question to determine Veteran status. To date 383 men 25 – 65 years old, reported Veteran status. Eight five were Veterans, 298 were non-Veterans. We continue to collect data.
Results: A comparison by Veteran status reveals that Veterans are more likely to be married (45% versus 66%, p=.004), educated (92% versus 72%, p=.0001) and to have insurance (56% versus 35%, p= .0003). In terms of medical care, 80% of Veterans had a physical checkup within the last 12 months or had seen a doctor within the last six months compared to 70% of non-Veterans (p=.07). Twenty six percent of the Veterans reported symptoms of depression compared to 15 % of non-Veterans (p=.02). Forty nine percent of Veterans reported having 4 or more drinks in a single day within the last 30 days compared to 40% of non-Veterans (ns). There were also no significant differences in the proportion of Veterans versus non-Veterans who used Ecstasy, cocaine, marijuana, amphetamines, heroin, inhalants or hallucinogens.
Conclusions: This is a snap-shot of an ongoing innovative data effort from a community sample that includes Veterans. Veterans had more depression, but no significant difference in drug use. Rather, Veterans reported more advantages than non-Veterans, including education, marriage, insurance and medical care. Based on national statistics, indicating that 1 in 4 homeless are Veterans, we expected Veterans to have less advantage than those in the general community.
Financial Support: NCRR UL1 RR0204992 ; T32 DA 07313

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GABRA2 AND PARENTAL CONTROL IN RELATION TO ADOLESCENT SUBSTANCE USE: THE TRAILS STUDY.

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Aims: One of the candidate genes implicated in substance use disorders is GABRA2. This study aimed to test 1) if genotypic variation in GABRA2 also contributes to adolescent substance use, and 2) whether parental control, adjusted for child disclosure, modifies the association between GABRA2 and adolescent substance use. We hypothesized moderation of the genetic effects by parental control, making carriers of the genetic risk markers most vulnerable to the influence of less optimal parenting.
Methods: Data from 1194 participants of TRAILS, a prospective general population study of Dutch adolescents, were analyzed. Self-reports completed at age 15-18 were used to obtain information on frequency of alcohol, nicotine and cannabis use, and on parental control and child disclosure. In the vast majority of cases, DNA was extracted from blood samples. Six SNPs in GABRA2 were analyzed. A latent substance use variable was created, and analyses were performed separately for males and females.
Results: A direct association between GABRA2 and substance use involvement was found, though only in males (rs3849591). Parental control was only associated with female substance use involvement and this association was found to be significantly stronger in carriers of the risk allele in one of the SNPs (rs2119183).
Conclusions: The results of this study confirm earlier reports of gender differences in the relation between GABRA2 and substance use, demonstrate some direct associations between GABRA2 and adolescent male substance use, and indicate that GABRA2 affects the influence of parental control on female substance use involvement.
Financial Support: TRAILS has been financially supported by various grants from the Netherlands Organization for Scientific Research, the Sophia Foundation for Medical Research, the Dutch Ministry of Justice, the European Science Foundation, and all participating universities.

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VIVITROL USE IN LOS ANGELES COUNTY.

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Aims: The aims were to evaluate the use of Vivitrol examining client retention, reduction in cravings, side effects, and counselor attitudes.
Methods: Three agencies were selected to administer the medication: Tarzana Treatment Center, Behavioral Health Services, and Prototypes. Data included the Urge to Drink Scale, Medication-Assisted Treatment survey (MAT), and the Counselor Survey on Medication-Assisted Treatment (pre and post surveys). Clients completed the Urge to Drink and MAT every week for the first four weeks and monthly following the second and subsequent doses. The counseling staff completed the Counselor Survey at the time of implementation and a post survey was completed four to five months later.
Results: About 60% of the clients were retained (given a second shot). Urges to drink decreased from an average of 15.9 to 7.7. Minimal side effects were reported. According to the pre Counselor Survey, approximately 40% had negative views of medication or reported that they did not know much about medication-assisted treatment. Counselors commented that clients on medication are not "sober" or that the use of medications should occur only when no other treatment is effective. Post survey results indicated that attitudes towards medication-assisted treatment improved and knowledge of medication-assisted treatment increased.
Conclusions: Counselor education and client support appear to be very important in the effort to help clients remain on Vivitrol for second and subsequent doses. The decrease in urges to drink may also have an impact on client outcomes whereby clients who remain on the medication are also more likely to remain in treatment. Overall, the use of medications appears to be an effective tool in the treatment of substance use disorders.
Financial Support: The Los Angeles County Department of Public Health, Substance Abuse Prevention and Control supported this research.

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AN ECONOMIC EVALUATION OF A PAPERWORK BURDEN REDUCTION INITIATIVE.

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Aims: While burdensome and unnecessary paperwork has been shown to adversely affect case managers and other treatment staff, the financial toll that is also placed on treatment programs has not been calculated. In addition, many administrators may be hesitant to make substantial changes to their paperwork process due to the limited time and financial constraints placed on their staff. However, additional information regarding the cost savings associated with these changes may show that these savings offset any initial costs required to review and modify their current paperwork systems. In 2007, the Delaware Division of Substance Abuse and Mental Health, with the help of the Treatment Research Institute, completed a statewide analysis of their paperwork system and recommended changes to both the process and scope in which client paperwork was administered. This is an economic evaluation of this process to determine the approximate costs and subsequent benefits that resulted from this paperwork burden initiative.
Methods: In addition to reviewing the data collected in the paperwork burden project, Directors and Program Managers from all participating treatment locations were interviewed in order to collect accurate economic costs and outcomes data for both the treatment staff and research team involved in the implementation of the paperwork burden project.
Results: The results of this economic review found that the implementation of recommendations from the original paperwork initiative led to a per client savings of $89.60 to the treatment center in regards to staff time saved for an average annual savings of $39,382 per treatment site and $196,913 across all treatment sites. These economic savings more than offset the cost incurred by the treatment sites and research team in the evaluation and implementation of the paperwork burden project ($14,471).
Conclusions: These results, combined with the overall positive feedback from treatment staff, support the need for periodic reviews and possible state-wide standardization of paperwork requirements.
Financial Support: This research was supported by NIDA grant #R21-DA019787.

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BUPRENORPHINE TREATMENT AND GENDER DIFFERENCES FOR INDIVIDUALS UNDER CRIMINAL JUSTICE SUPERVISION: A PILOT STUDY.

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Aims: Buprenorphine has been shown to be widely effective for the treatment of opioid dependence. However, no studies have examined gender differences in response to treatment and few studies have examined the impact of treatment among individuals under community corrections supervision.
Methods: 30 men and women under community supervision were recruited onsite from community corrections offices. Seventeen women and 13 men were enrolled and provided urine drug screens (UDS), received study medication dispensed weekly over 12 weeks, weekly medication management therapy, and returned for a one month follow-up. Intent-to-treat analyses were performed for all time points through follow-up.
Results: The majority of participants were Caucasian (90%), young (M=31.7+7.4), never married (43.3%), with at least a high school/GED education (80%). Over half (53%) were HCV+. GEE analyses showed an interaction effect between gender and time (p=0.008). Point prevalence opiate positive UDS were initially similar at study enrollment but by week 10 men were generally 15-20% higher on UDS compared to women and by EOT, 77% of men and 59% of women participants were positive for opiates. Across all UDS, women were more likely to test positive for benzodiazepines (53% vs. 18%; p=0.004) but had similar UDS results for other illicit drugs compared to men. Treatment retention and average buprenorphine dose were similar between gender groups.
Conclusions: This initial pilot study found a significant interaction effect across treatment between men and women, with men having higher rates of positive UDS for opiates by EOT compared to women. This may suggest the need for tailored interventions to address the heightened drug use by men, particularly approaching the time of taper. More intensive psychosocial strategies, in conjunction with buprenorphine treatment, may be needed to provide the most effective treatments for men and women under criminal justice supervision.
Financial Support: Supported by UAB Psychiatry Departmental Funds

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

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Aims: When deciding between doing a risky behavior (e.g., drug use, a criminal act, sex) with chances for either big rewards or losses, vs. a cautious behavior with small rewards but no losses, youths with antisocial substance disorder (ASD; substance use disorder plus conduct disorder) often choose the former. Extending our earlier fMRI observations as boys repeatedly decided between doing a risky or a cautious behavior (Crowley et al 2010), we now ask, do ASD boys and controls differently process decisions leading to cautious behaviors; do they differently process decisions leading to risky behaviors?
Methods: Adolescents (20 ASD patients, 20 controls) played a computer game. In each of 90 decision trials subjects decided between making a cautious response (win 1 cent) or a risky response (win 5 or lose 10 cents; odds of losing increased as the game progressed). fMRI results were compared with 90 similar trials requiring no decisions.
Results: In this simple task the groups behaved similarly. But in deciding to do a cautious response controls activated 2121 voxels (mean), while patients activated 140; controls' significantly greater activation included DLPFC, ACC, insula, OFC, cerebellum, and other regions. When deciding to do a risky response controls activated 4070 voxels, and patients activated 2177; controls' significantly greater activation included cerebellum, right frontal pole, and temporal and parietal structures. Before risky responses both groups' mesolimbic DA systems activated, but similarly.
Conclusions: The groups behaved similarly, but their brains functioned differently. To decide upon a cautious response controls recruited about 15-fold more voxels than patients, including regions selecting among possible behaviors based on changing reinforcement schedules and assessments of future punishments. ASD patients' utilization of brain regions that make cautious choices was severely deficient. Before risky responses the two groups' DA-system activation was similar, but they differed in other regions.
Financial Support: NIDA: DA 009842, 011015

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THE EPIDEMIOLOGY OF COCA LEAF CHEWING: MENTAL HEALTH SURVEY EVIDENCE FROM THE RURAL ANDEAN HIGHLANDS OF PERU, 2008.

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Aims: The still-widespread ancient Andean custom of chewing leaves of Erythroxylum coca is an under-studied facet of drug epidemiology in Latin America. Here, the aim is to study coca chewing (CC) and to estimate occurrence of coca dependence (CD) in relation to individual level characteristics such as ethnicity and exposure to political violence (EPV; e.g., Shining Path terrorism).
Methods: Data are from mental health surveys conducted by our institute in the rural highlands of Peru (n= 3,031 adults 18+ years). Standardized assessments covered coca leaf chewing and dependence (via MINI neuropsychiatric interview), age, education, ethnicity, and EPV levels. The statistical approach deals with complex survey design features.
Results: An estimated 4 in 10 adult residents of these Peruvian highland rural communities have chewed coca leaves, with roughly 1 in 4 chewing coca in the 12 months before assessment. Among lifetime CC users, an estimated 1 in 2 have used recently, in the prior 12 months, and among these recent users, 0.9% qualify as cocaine dependence cases (95% confidence interval = 0.5%, 1.4%). CD is associated with older age, ethnic affiliation (Quechua), lower educational attainment, and higher EPV ($p<0.05$).
Conclusions: The custom of coca leaf chewing is prevalent, is not distributed at random in the Peruvian highlands under study, and is not often complicated by cocaine dependence as assessed via the MINI. The observed associations describe epidemiological features that deserve attention in future public health research in Peru.
Financial Support: NIH/FIC/NIDA D43TW05819 & K05DA015799.

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A LOW-DENSITY GENE ARRAY ASSOCIATION STUDY IMPLICATES DIFFERENT PATHWAYS IN PRIMARY AFFECTIVE DISORDERS VS. THOSE COMORBID WITH SUBSTANCE DEPENDENCE.

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Aims: Affective disorders (AFDs) commonly co-occur with substance dependence (SD). We examined and compared risk genes and potential networks for primary AFDs (PAFDs) and AFDs comorbid with SD (CAFDs).
Methods: We genotyped 1350 SNPs in or near 130 genes in 868 European-Americans (182 PAFDs, 214 CAFDs and 472 controls) via Illumina GoldenGate Array. We analyzed pathways and functions with the IPA program.
Results: GSK3B, GRIK1, SLC18A2, and NGFB were associated (i.e., at least one SNP p [empirical] <0.001) with PAFDs; GSK3B was most strongly associated. DBH, ADH6, ADH1A, SLC6A12, GRIN2B, PPP1R1B, and EIF4ENIF1 were associated with CAFDs; EIF4ENIF1 and SLC6A12 were most strongly associated. IPA analysis indicated that the pathways associated with PAFDs included behaviors (global p=3.44E-16; including spatial learning, recognition, and memory), neuronal proliferation, growth, apoptosis, and hyperalgesia. Similarly, pathways associated with CAFDs were psychological diseases, neurological diseases, and organismal injury and abnormalities. The traits whose pathways were most closely related were alcoholism (p=1.17E-12) and major depression (p=1.50E-12). Canonical pathway analyses by IPA program showed that dopamine, 5-HT, GABA, and second messenger signaling were significantly associated with both PAFDs and CAFDs, but amino acid and carbohydrate metabolism signaling were associated with CAFDs only.
Conclusions: PAFDs and CAFDs have both unique and shared risk factors and biological pathways.
Financial Support: VA CT REAP Center; NIH grants AA11330, DA12849, DA18432, DA12690

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CALCIUM SIGNALING UNDERLYING NICOTINE'S SUPPRESSIVE EFFECT ON TLR3 AND TLR4 PATHWAYS.

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Aims: Nicotine, a critical component of tobacco smoke, exerts anti-inflammatory effects in multiple immune cells by suppressing the expression of lipopolysaccharide-induced pro-inflammatory cytokines. However, how nicotine regulates the Toll-like receptor (TLR) pathways has not been fully understood. The goal of this study was to determine how nicotine regulates TLR signaling pathways and their underlying mechanisms.
Methods: We challenged mouse macrophages with ligands for different TLRs, including TLR3 and TLR4, and measured expression of 40 key genes in the TLR pathways by real-time PCR array. In addition, we employed conventional molecular biology techniques, such as Western blotting and ELISA, to verify some of the significant findings. Moreover, we determined the calcium signaling promoted by TLR ligands after nicotine treatment with calcium imaging, antibody array, and Western blotting techniques.
Results: Expression of multiple adaptors was significantly suppressed by nicotine. Nicotine impacted the TRIF-dependent pathway more than the MyD88-dependent pathway. Finally, TLR-promoted calcium release, and the phosphorylation of calcium-pathway-related kinases can be significantly suppressed by nicotine.
Conclusions: Nicotine has extensive suppressive effects on TLR signaling, although the impact differs between TRIF- and MyD88-dependent pathways. Calcium signaling is involved in nicotine's regulatory effect.
Financial Support: This study was supported in part by National Institutes of Health grants DA-12844 and DA-026356, and China Scholarship Council to WYC.

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DIFFERENCES BETWEEN NFL PLAYERS WHO OBTAIN THEIR OPIOIDS FROM DOCTORS ONLY VS. ILLICIT SOURCES.

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Aims: This analysis explores differences in health and reasons for prescription opioid use between retired NFL football players who obtained prescription opioids from doctors only during their NFL play compared to those who obtained prescription opioids from illicit sources.
Methods: We conducted a national telephone survey of 1,788 former NFL football players in order to better understand their health concerns, pain levels, and methods of pain management. Of the players surveyed, 1,184 were eligible for study participation, 644 (54.4%) of whom completed the survey. Only 336 players (52.2%) reported using prescription opioids during NFL play.
Results: Players who obtained their opioids from an illicit source during their tenure in the NFL (N=211) were significantly more likely to report moderate to severe mental impairment from NFL injuries (30% vs. 16%, p=.005) than players who obtained opioids from their doctor only (N=125). No significant differences were found between players who obtained their opioids from a doctor only vs. those who obtained them from an illicit source with respect to number of injuries received in the NFL, number of concussions, or level of pain. When reasons for use were examined, players who obtained their drugs illicitly versus those who obtained them from a doctor only were more likely to use prescription opioids to get high (11% vs. 3%, p=.012), to relieve stress (22% vs. 6%, p<.0001), and to sleep (35% vs. 20%, p=.003).
Conclusions: Professional athletes who obtain prescription opioids from illicit sources are at greater risk for mental impairment. The fact that use from a doctor only is not related to more injuries, more concussions, and more pain could be attributed to players' unwillingness to divulge their conditions to their physicians out of fear of being grounded from play. Better medical attention for players' problems related to stress and sleep management could mitigate the amount of prescription opioid misuse that occurs.
Financial Support: ESPN and NIDA funded (LB Cottler, PI)

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NICOTINIC α4β2 RECEPTORS AND THE DISCRIMINATIVE STIMULUS EFFECTS OF NICOTINIC RECEPTOR AGONISTS IN RHESUS MONKEYS.

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Aims: To examine the in vivo pharmacology of nicotinic receptor ligands in rhesus monkeys, with an emphasis on involvement of α4β2 nicotinic receptor subtypes, nicotine and other nicotinic agonists currently used as smoking cessation pharmacotherapies (i.e., varenicline and cytisine) were studied alone and in combination with the α4β2 nicotinic antagonist dihydro-β-erythroidine (DHβE).
Methods: Monkeys (n=5) discriminated nicotine (1.78 mg/kg, s.c.) from saline under a fixed ratio 5 schedule of stimulus-shock termination. Dose-response functions were determined for nicotine, varenicline, and cytisine to produce discriminative stimulus effects. DHβE was studied alone and in combination with nicotine and varenicline.
Results: Nicotine, varenicline, and cytisine dose-dependently increased nicotine-lever responding to >80% in 5/5, 5/5, and 4/5 monkeys, respectively. The ED50 values (95% confidence limits) were 0.63 (0.39-1.0), 0.57 (0.35-0.92), and 38.7 (23.5-63.8) mg/kg, respectively. In contrast, DHβE (1 and 3.2) produced a maximum of 25% nicotine-lever responding. DHβE (3.2 mg/kg) did not significantly modify the dose-response function of either nicotine or varenicline. These results contrast with previous studies in these same monkeys showing that the non-selective nicotinic receptor antagonist mecamylamine (1 mg/kg) produced 3.2- and 3.3-fold rightward shifts in the nicotine and varenicline dose-response functions, respectively.
Conclusions: Nicotine, varenicline, and cytisine are able to produce the same maximum effect. Moreover, in primates, both cytisine and DHβE have markedly lower potency than expected according to their potency relative to nicotine and mecamylamine, respectively, in rodents. DHβE appears to be a relatively ineffective nicotinic antagonist in primates. Alternatively, these data could challenge the widely-accepted view that α4β2 nicotinic receptors predominantly mediate effects underlying the abuse liability of nicotine.
Financial Support: Supported by USPHS grant DA25267

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REGULATORY COMPLIANCE OF RESIDENTIAL TREATMENT CLINICS IN WEST CENTRAL MEXICO.

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Aims: In 2009, Mexico updated the NOM 028 (official Mexican norm) for the prevention, treatment and control of addictions. This study examined NOM 028 compliance among residential treatment clinics in Mexico's west central state of Jalisco.
Methods: We conducted an on-site survey of all 191 residential clinics in Jalisco, and examined the 15 most relevant NOM 028 regulatory requirements, including registration, opening notice, inspection visit, medical liability, medical registration, county license, and national addiction council (CONADIC) registration. We also surveyed the physical condition of facilities. Each of the 15 requirements was scored for compliance using a 5-point index: extremely bad, bad, sufficient, good and excellent. The type/modality of clinics was: 77% self-help, 17% combined medical/self-help (M/SH), 5% medical, 1% alternative.
Results: None of the clinics received excellent ratings on all 15 regulatory aspects. The combined index score for regulatory and physical condition resulted in good compliance for only 22.2% of medical clinics, 18.8% of M/SH clinics and 4.7% of self-help clinics. The medical and M/SH clinics had higher scores than the self-help clinics primarily due to better compliance on medical and psychological evaluations and facilities' physical condition. Clinic type/modality differed little regarding items such as knowledge of the NOM, medical liability, inspection visit, and opening notice.
Conclusions: None of the clinics fulfilled 100% of the NOM 028. Although medical and combined M/SH clinics received higher index scores, this was due primarily to better ratings on a few aspects of the regulations. Regardless of type/modality, only a small percentage of clinics received good overall compliance scores. The findings indicate a need for NOM 028 compliance training in clinics throughout Jalisco.
Financial Support: State Council for Addictions of Jalisco

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KNOCKDOWN OF 5-HT2C RECEPTOR IN THE NUCLEUS ACCUMBENS ENHANCES TRAIT IMPULSIVITY AND CONFERS ENHANCED SENSITIVITY TO NON-DRUG REWARD.

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Aims: Serotonin (5-HT) is important in the control over the affective and motivational aspects of palatable food reward. The 5-HT2C receptor (5-HT2CR) regulates neurobehavioral processes which may underlie important chronic health maladies including obesity, eating disorders and drug addiction. Impulsivity is a multifaceted personality trait that is broadly defined as action without sufficient foresight and functions both as a predisposing factor and consequence of addiction. The purpose of this study was to assess the role of nucleus accumbens shell (NAcSh) 5-HT2CR in sensitivity to natural reward as well as expression of impulsivity and compulsivity endophenotypes.
Methods: Recombinant AAV vectors were constructed with a separate expression cassette for eGFP and shRNA directed at the 3' untranslated region of the rat 5-HT2CR to decrease expression of all endogenous 5-HT2CR isoforms. The 5-HT2CR shRNA-AAV-eGFP viral vector was bilaterally infused into the NAcSh of male rats, while control animals received bilateral intra-NAcSh infusions of AAV-eGFP. All animals were subjected to the sucrose two-bottle choice and 1-choice serial reaction time tasks.
Results: Knockdown of NAcSh 5-HT2CR increased preference for 1% sucrose solution vs control. Exposure to a sub-preference concentration of sucrose (0.05%) following 4 days withdrawal resulted in sucrose preference in rats with a loss of NAcSh 5-HT2CR. Premature responses were elevated in 5-HT2CR knockdown rats, indicating enhanced impulsivity.
Conclusions: Sensitivity to non-drug reward is enhanced following knockdown of the 5-HT2CR in the NAcSh. 5-HT2CR in the NAcSh may play a role in regulation of responsiveness to rewarding stimuli and exerts inhibitory control over trait impulsivity.
Financial Support: Jeane B. Kempner Scholarship, DA06511, DA024157, DA020087, DA000403

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PIPERAZINE CONTAINING PARTY PILLS—EFFECT OF AN ACUTE DOSE OF TRIFLUROMETHYLPHENYLPIPERAZINE ON EXECUTIVE FUNCTIONING USING THE STROOP PARADIGM.

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Aims: Trifluromethylphenylpiperaizne (TFMPP) is one of the major constituents of a relatively new group of designer drugs which were marketed as safe and legal alternatives to illicit recreational drugs. This study is a randomized double blinded cross-over trial to determine the effects of TFMPP on impulse control and executive function in comparison to placebo using fMRI
Methods: 12 healthy subjects aged 18-40 were imaged by fMRI. Imaging was performed whilst subjects completed a Stroop paradigm 90minutes after an oral dose of TFMPP (50mg) 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).
Results: Response time (RT) and accuracy during the Stroop task were analyzed using repeated-measures ANOVAs and SPM8 was used to identify regional activation during the three Stroop conditions. Analysis of the overall Stroop (incongruent-congruent) condition (puncorr<0.001) resulted in significant change in activation for both the placebo and the TFMPP group in the cingulate cortex (CC) and right inferior cortex (rIFC), however the activation in placebo group was more accentuated in both areas. Placebo also activated the caudate. There were no significant differences were found for both RT and accuracy.
Conclusions: This study is the first to investigate the effect of TFMPP on cognition and executive functioning using fMRI. The group taking placebo have displayed an increased number of areas of activation relative to those who have taken TFMPP in the CC and rIFC and additional activation in the caudate. These results suggest that TFMPP decreases response inhibition when faced with conflict.
Financial Support: School of Pharmacy, The University of Auckland

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ABSENCE OF GENDER DIFFERENCES IN TREATMENT WITH RELAPSE PREVENTION MEDICATIONS FOR OPIOID DEPENDENCE IN YOUTH.

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Aims: This study describes the association between gender and medication treatment over 26 weeks in youth with opioid dependence in a community treatment program.
Methods: Data was abstracted retrospectively from clinical charts of 133 patients admitted between 4/07 and 1/10 to the adolescent/ young adult outpatient opioid track at Mountain Manor Treatment Center in Baltimore MD.
Results: Patients were 54% male, 94% Caucasian, mean age 18.2. Females and males were similar in regards to mean age (18.1 years vs 18.2 years), mean duration of opioid use (2.6 years vs 2.9 years), rates of injection use (60% vs 62%); rates of use of any pharmacotherapy (56% vs 63%); rates of use of buprenorphine (32% vs 45%); rates of use of extended release naltrexone (19% vs 18%). For those on no medication, mean cumulatative retention was 10.3 weeks. Both males and females on medications had longer mean cumulative retention without substantial gender differences – females on buprenorphine had 16.4 weeks vs males with 15.5 weeks; females on extended release naltrexone 14.9 weeks vs males with 17.6 weeks. For those on no medication mean cumulative time without opioid use (combining self-report and urine testing) was 7.0 weeks. Both males and females on medications had more cumulative opioid free weeks with minor gender differences – females on any relapse prevention medication had 9.5 weeks vs 10.7 weeks for males; females on buprenorphine had 8.7 weeks vs 11.3 weeks for males; females on extended release naltrexone had 12.4 weeks vs 9.2 weeks for males.
Conclusions: In this high severity group of opioid dependent youth there were no gender differences in rates of treatment presentation or clinical characteristics. Without substantial gender differences, the use of medications for relapse prevention was associated with increased retention and opioid free weeks. Both female and male youth appear to respond positively to pharmacotherapy for opioid dependence over the 1st 26 weeks of treatment in this retrospective, non-randomized sample.
Financial Support: Mountain Manor Treatment Center.

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ENRICHING ATTITUDES OF PSYCHIATRY RESIDENTS TOWARD PEOPLE WITH SUBSTANCE USE DISORDERS.

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Aims: To document the shift in attitudes of psychiatry residents toward people with substance use disorders (SUD) before and after exposure to a 2-week outpatient substance abuse treatment rotation.
Methods: Residents prepared a reflective narrative account describing their experiences with individuals (including patients) with SUD, on the first and last day of the rotation. The writing samples were de-identified and decoupled from their pre/post pairings and analyzed using a narrative analysis technique for four continuums of views of SUD: 1) acute v chronic illness; 2) moral failure v complex behavioral disorder; 3) treatment nihilism v therapeutic hopefulness; and 4) low v high empathy. A scoring rubric for possible attitudes on those continuums was agreed upon by a group of 4 faculty members and a child psychiatry fellow in the departments of psychiatry and pediatrics. Specific language was identified in each narrative to score the four continuums. Scores were assigned to each narrative by group consensus.
Results: All 15 residents completed the exercise and the reflective writings were evaluated utilizing narrative analysis. Analysis showed movement in every domain in a more complex direction and the 'treatment nihilism v therapeutic hopefulness' domain was most affected.
Conclusions: The attitudes of first year psychiatry residents shifted toward more complex views of SUD along the four continuums after exposure to an outpatient substance abuse treatment rotation. These enriched attitudes may improve treatment of persons afflicted by SUD. Further study is required to determine why there was a lack of significant change in the 'moral failure v complex behavioral disorder' domain. A secondary finding is that requiring a repeated narrative writing assignment is a useful tool for evaluating attitudes of medical trainees and is applicable in a wide range of educational settings.
Financial Support: The Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, School of Medicine

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CHRONIC PAIN AND OFFICE-BASED BUPRENORPHINE-NALOXONE TREATMENT OUTCOMES.

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Aims: The impact of chronic pain (i.e., pain lasting at least 3 months) on office-based buprenorphine-naloxone treatment (BNT) is currently unclear. This study explored (a) differences in baseline characteristics and treatment outcomes between those with and without chronic pain and (b) changes in pain ratings during treatment.
Methods: Participants were 88 opioid dependent individuals receiving BNT as part of a 6-month randomized clinical trial. Baseline and monthly assessments included the Addiction Severity Index (ASI) and measures of pain intensity, pain interference, and treatment satisfaction. Urinalysis was conducted weekly.
Data Analysis: All analyses were conducted using mixed-model repeated-measures analysis of variance, using an autoregressive covariance structure.
Results: Of the 88 participants, 28 (32%) reported chronic pain (CP) at baseline. Compared to the no chronic pain patients (NCP), CP patients were less likely to be employed (36% vs. 62%, p=.04) or to report heroin as their primary drug of abuse (50% vs. 77%, p=.02), and were more likely to report higher current and past month pain intensity (p's <.001). CP and NCP groups did not differ on any other demographic or baseline variables, including the ASI, or on the treatment outcomes of weeks retained in treatment (18.7 vs. 17.6, p=.54), treatment completion (39% vs. 35%, p=.81), maximum consecutive weeks of opioid-free urines (6.4 vs. 6.5, p=.98) or treatment satisfaction (p=.35). For both the CP and NCP groups, average pain intensity and interference significantly decreased during treatment as compared to baseline (p=.001).
Conclusions: Chronic pain is prevalent among patients entering BNT, improves with treatment, but is not associated with poorer outcomes.
Financial Support: Supported by NIDA K23 DA024050, K24 DA00445, K01 DA022398, and R01 DA019511

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ESTABLISHMENT OF INTER-OBSERVER RELIABILITY USING THE FINNEGAN NEONATAL ABSTINENCE SCORING TOOL.

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Aims: The aims of this program are to train healthcare professionals and researchers to assess neonates for signs and symptoms of abstience with accuracy and decrease subjectivity when using the FNAST in the clinical area.
Methods: This is an inter-observer reliability program that includes a manual, demonstration exam, two infants being assessed for signs and symptoms of abstinence and a review of the exams pointing out the signs and symptoms present. The demonstration DVD and exam reviews are narrated. Partitipants watch the exam, score the infant using the FNAST and watch the exam review. Then participants check their inter-observer reliability using a percent agreement chart. To be reliabile in using the tool participants must obtain 90% agreement or greater.
Results: This program has been used to train staff nurses to improve their inter-observer reliability using the FNAST. An inter-observer reliability score of 90-100% has been achieved when using this program.
Conclusions: The incorporation of this program into practice will allow healthcare professionals to become more proficient in assessing neonatal abstinence and neonates will receive the appropriate treatment to control signs and symptoms of neonatal abstinence.
Financial Support: None

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INCREASED SERUM BRAIN-DERIVED NEUROTROPHIC FACTOR IS PREDICTIVE OF COCAINE RELAPSE OUTCOMES: A PROSPECTIVE STUDY.

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Aims: Cocaine dependence is associated with high relapse rates but few biological markers associated with relapse outcomes have been identified. Extending preclinical research implicating brain BDNF as a mediator in stress-related cocaine seeking, we examined whether serum Brain Derived Neurotrophic Factor (BDNF) is altered in abstinent, cocaine dependent (CD) individuals and if it is predictive of subsequent relapse risk.
Methods: Serum samples were collected across three consecutive mornings from 35, treatment-engaged CD patients (17M/18F) and 34 healthy control (HC) participants (17M/17F) and BDNF levels were assessed using the enzyme-linked immunosorbent assay while both groups were in an inpatient setting. CD individuals were prospectively followed for 14, 30 and 90 days post-treatment discharge to assess cocaine relapse outcomes. Time to cocaine relapse, number of days of cocaine use (frequency), and amount of cocaine use (quantity) were the main outcome measures.
Results: High correlations in serum BDNF across days indicated reliable and stable serum BDNF measurements. Significantly higher mean serum BDNF levels were observed for the CD patients compared to the HC participants ($p<0.001$). Serum BDNF levels predicted time to cocaine relapse (hazard ratio: HR: 1.09, $p<0.05$), total amount of cocaine used per occasion ($t = 2.05$, $p= 0.05$) and number of days of cocaine use ($t = 2.16$, $p= 0.04$) in the follow-up period.
Conclusions: Higher serum BDNF levels in cocaine abusers relative to controls may reflect cocaine withdrawal-related adaptations. Furthermore, associations between higher serum BDNF and relapse outcomes suggest that changes in serum BDNF are clinically relevant. These data support the need to target normalization of BDNF levels during cocaine recovery to improve relapse outcomes in cocaine dependence.
Financial Support: P50-DA016556 and PL1-DA024859

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DOES SEX, AGE AND DRUG HISTORY AFFECT BEHAVIORAL RESPONSES TO LOW-DOSE MDMA AND AMPHETAMINE IN A SENSITIZATION PARADIGM?

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Aims: Previous studies have demonstrated that behavioral sensitization may develop following low dose administrations of MDMA in the rat. We investigated whether age, sex and drug history would influence the development or expression of sensitization.
Methods: 60 Sprague-Dawley rats (33 female), grouped according to sex, age (young<6 months; old > 20 months) and drug history (drug naïve or 15 month MDMA/amphetamine drug discrimination), were injected (i.p.; 20 min ptt) with drug/saline and locomotor activity was measured for 60 min at 28°C. Two groups (young male/female controls) received three once-weekly injections of saline while six groups (young male/female, old drug naïve male/female and old drug history male/female) received three once-weekly injections of 5mg/kg MDMA. Contextual sensitization was evaluated at Week 4, as was cross-sensitization to d-amphetamine (0.56mg/kg; Week 5).
Results: During habituation, females showed greater spontaneous locomotor activity than males; there was no effect of age or history. MDMA increased locomotor activity but there was no evidence of a sensitized locomotor response in any MDMA-treated group. With respect to response to MDMA, there were significant effects of age and history (but not sex), with older MDMA-treated rats having a greater locomotor response and rats with a MDMA/ amphetamine drug history having a greater overall response to MDMA. In the test for contextual sensitization, there was an effect of age (but not sex or history), with young rats more active in the open field apparatus. The amphetamine challenge showed that young rats (females in particular) and old drug history males had significantly greater locomotor responses.
Conclusions: Females had greater spontaneous locomotor activity and sensitivity to amphetamine challenge; age and drug history predicted a greater locomotor response to MDMA. Despite differences in sex, age and history, this sensitization paradigm, used successfully elsewhere, did not result in behavioral sensitization in any group in our study.
Financial Support: This project received no external funding support

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DISTRESS TOLERANCE AND NEGATIVE MOOD REGULATION EXPECTANCIES PREDICT ADOLESCENT SMOKING SELF-CHANGE EFFORTS.

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Aims: More than half of adolescent smokers report previous attempts at changing their smoking behavior, but only a small percentage actually succeed in quitting smoking (YRBS, 2005; Riedel et al., 2002; Moss, Allen, Giovino & Mills, 1992; Zhu et al., 1999). The present study, investigated the degree to which the relationship between distress tolerance and negative mood regulation expectancies contribute to poorer smoking outcomes following a quit attempt.
Methods: The study is currently in the data collection process. The available sample consists of 46 adolescent daily smokers who reported a desire to quit smoking within 30 days upon enrollment (mean age =17.3, 50% male, 61% White, mean cigarettes per smoking day (CPSD) = 8.0). 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 was measured using the Mirror Tracing Persistence Task (MTPT), a computer-based behavioral task.
Results: To date, 72% of participants reported making a quit attempt (mean duration = 13.5 days) and 76 % of participants indicated a reduction of CPSD. Lower distress tolerance as assessed by the MTPT was associated with lower mood regulation expectancies (r =.53) and higher baseline CPSD (r = -.30). Hierarchical linear modeling (HLM) analyses of smoking reductions over time indicated that after including baseline CPSD and gender and the effect of time, that greater negative emotional regulation expectancies (B = .10, SE = .05, p = .04) accounted for the association between lower distress tolerance (B = -.003, SE = .004, p = .99) and subsequent smaller reductions in CPSD across the follow-up period.
Conclusions: Low psychological distress tolerance as it relates to negative mood regulation expectancies should be considered as a basic mechanism to target in smoking interventions for adolescents.
Financial Support: NIDA K23 DA23143

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MINDFULNESS-BASED PSYCHOTHERAPY FOR CANNABIS OR COCAINE DEPENDENCE.

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Aims: Mindfulness training represents a novel direction in drug treatment, particularly for those inclined towards non-medication based approaches. Mindfulness refers, most generally, to the capacity for acceptance, neutrality, non-reactivity, and sustained attention, and mindfulness training typically occurs in a didactic, group-based format geared towards teaching various meditation exercises. In this study, the feasibility of a 10-week individual mindfulness-based psychotherapy, tailored to the drug-using population and modeled on mindfulness-based stress reduction (MBSR), was explored in treatment-seeking cannabis or cocaine dependent individuals.
Methods: 25 individuals meeting entry criteria and seeking treatment for cocaine or cannabis dependence provided consent for study participation. Weekly individual mindfulness training coupled with psychotherapy was provided, as well as weekly ratings and drug tests. The psychotherapy was supportive, goal-directed, and oriented around helping participants incorporate mindfulness exercises into their daily lives. After completion of the 10 week study, patients returned 4 weeks later for follow-up.
Results: 11 of the 25 enrolled patients were cocaine dependent, while 14 of the patients were cannabis dependent. There were 19 completers overall (76%): 8 in the cocaine group, of whom 6 (55%) were abstinent (no use for 2 weeks by self-report and urine toxicology) at the end of study and at follow-up, and 11 in the cannabis group, of whom 8 (57%) were abstinent at the end of study and at follow-up. Changes in various measures – mindfulness, spirituality, and self-efficacy ratings – were also documented.
Conclusions: While one cannot draw any conclusions about efficacy from this non-controlled trial, the findings demonstrate that individual mindfulness-based psychotherapy was well tolerated, helpful for a majority of patients, and associated with high retention rates in both groups. Future studies might consider incorporating a control group to test the efficacy of this potentially therapeutic strategy.
Financial Support: NIDA grants T32 DA007294015 (Levin) and P50-DA009236 (Kleber).

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ILLICIT USE OF BUPRENORPHINE AMONG YOUNG ADULTS IN OHIO.

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Aims: There is growing evidence about illicit use of Suboxone (buprenorphine/naloxone) and Subutex (buprenorphine) in the US. The study aims to: 1) identify predictors of illicit buprenorphine use in a community sample of 400 young adults with a recent history of illicit pain pill use; 2) describe knowledge, attitudes and behaviors linked to illicit buprenorphine use as reported by a qualitative sub-sample (n=52).
Methods: Participants were recruited using respondent-driven sampling. Eligibility criteria included: 1) illicit use of pain pills on at least 5 occasions in the past 90 days; 2) 18-23 years old; 3) no history of heroin or injection drug use; 4) no lifetime dependence on pharmaceutical opioids; 5) no current involvement in formal drug treatment. Qualitative interview participants were selected from the larger sample. Logistic regression analysis was conducted using SPSS. Thematic analysis of qualitative interviews was conducted using NVivo.
Results: The sample was 55% male and 50% white. Over 90% reported lifetime illicit use of oxycodone (excluding OxyContin) and hydrocodone, 44% had used OxyContin, 8.3% Suboxone and about 1% Subutex. White ethnicity, the intranasal inhalation of crushed pain pills, and lifetime illicit use of OxyContin and methadone were linked to increased odds of lifetime illicit use of buprenorphine. Qualitative interviews revealed that buprenorphine was more commonly used by more experienced users who were introduced to it by their "junkie friends." Those who used buprenorphine to self-medicate withdrawal referred to it as a "miracle pill." When used to get high, reported experiences ranged from "the best high ever" to "puking for days." Participants reported using Suboxone orally or by intranasal inhalation. Injection of Subutex was also reported.
Conclusions: Our findings suggest that illicit buprenorphine use is gaining ground primarily among whites and those who are more advanced in their drug use careers. This study is among the first conducted in the US to report on buprenorphine use for the purpose of intoxication.
Financial Support: Financial support was provided by NIDA (R01DA023577; Carlson, PI)

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GENDER-SPECIFIC RELATIONSHIP BETWEEN DISTRESS TOLERANCE AND HPA AXIS RESPONSE TO STRESS AMONG ADOLESCENTS.

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Aims: Low distress tolerance (DT), defined as the inability to persist in goal directed activity when experiencing emotional distress, is associated with poor adolescent outcomes such as increases in substance use. Evidence indicates that a gender specific HPA axis response to stress is also associated with internalizing and externalizing symptoms in adolescents, and therefore may underlie the relationship between DT and substance use. As a first step, the purpose of the current study was to examine the gender specific association between distress tolerance and HPA axis response to stress among adolescents.
Methods: 150 14-18 year old adolescents (M = 16.0, SD = 1.0; 52.8% Female, 54.3% African American) and their primary caregiver attended a 2 hour assessment session. Salivary cortisol samples were collected at baseline and at 10 minute intervals following exposure to a behavioral stress task. Distress tolerance was assessed with two computerized tasks, the PASAT and MTPT. Demographics and parent report of attention, externalizing, and internalizing symptoms were included as covariates.
Results: Salivary cortisol response to stress was analyzed as area under the curve (AUC) from baseline up to 40 minutes post stress exposure. Separate logistic regression analyses were conducted to predict distress tolerance on each task, with the AUC X Gender interaction term entered in the final step. Both models were significant, with the AUC x Gender interaction significantly related to distress tolerance on the PASAT-C (Wald = 9.22; $p < .01$; OR = 0.92) and MTPT-C (Wald = 6.60; $p < .01$; OR = 0.94). Low distress tolerance was associated with a significantly lower AUC among males, whereas females with low distress tolerance evidenced a higher AUC.
Conclusions: The current findings suggest that biomarkers for distress tolerance among adolescents may be gender specific. Implications and future directions will be discussed.
Financial Support: NIDA R21 DA022741 (PI: Daughters)

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PREDICTORS OF MODERATE, SUBSTANTIAL OR SEVERE PROBLEMS ASSOCIATED WITH DRUG ABUSE IN COLLEGE STUDENTS REPORTING RECENT NON-MEDICAL OPIOID USE.

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Aims: The RADARS® System College Survey Program (CS) provides an opportunity to evaluate predictors of increased abuse related problems as measured by the DAST-10. This research sought to evaluate risk factors of high DAST-10 scores associated with misuse and abuse of opioids in a population of college students.
Methods: 7892 college students sampled equally from 4 regions in the US completed an online questionnaire as part of CS (3Q2009, 4Q2009, 1Q2010, and 3Q2010). Respondents included in the analysis indicated non-medical opioid use within the past 3 months and completed a substance abuse screening instrument (DAST-10). DAST-10 scores were categorized as Low (DAST-10 None (1) & Low(2)) and High (DAST-10 Moderate(3-5), Substantial(6-8), Severe(9-10)). Potential risk factors for High DAST-10 scores were use of extended release (ER) opioids, methadone, hydromorphone, oxymorphone, multiple opioids, tobacco and alcohol. Additional covariates for gender, race/ethnicity and age were also included. Multiple logistic regression was used to assess associations between DAST-10 groups and the risk factors using a backward elimination selection procedure.
Results: 697 (8.8%) reported opioid drug use and completed the DAST-10. Covariates associated with High DAST-10 scores included male gender OR = 2.00 (95% CI: 1.41, 2.86); tobacco use OR = 1.86 (95% CI: 1.28, 2.71); ER use OR=1.65 (95% CI: 1.003, 2.93); hydromorphone use OR = 2.35 (95% CI: 1.32, 4.03); methadone use OR=1.93 (1.17, 3.23); and "multi-drug" use OR = 2.36 (95% CI: 1.42, 3.95).
Conclusions: ER opioids are associated with a 65% increased risk of High DAST-10, even after accounting for "multi-drug", hydromorphone and methadone use.
Financial Support: The RADARS System is a public non-profit organization providing post-marketing surveillance of prescription medications to pharmaceutical manufacturers.

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MANUFACTURE AND ANALYSIS OF REDUCED NICOTINE CIGARETTES FOR NIDA DRUG SUPPLY PROGRAM.

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Aims: Supplies of reduced nicotine cigarettes (RNCs) are being manufactured for the National Institute on Drug Abuse Drug Supply Program (NIDA DSP) for use in research programs. These supplies will be distributed according to standard DSP procedures.
Methods: As some previous commercial supplies have not been well received by research subjects, the development of the cigarettes includes a significant design phase, including consultation with a panel of investigators with expertise in the subject area. RTI is collaborating with 22nd Century Ltd in the design and manufacture of the RN cigarettes. With consultation from NIDA, the expert investigators, and 22nd Century, some 23 types of RNC were selected for manufacturing. These include cigarettes with nicotine delivery levels from 1.5 to <0.05 mg/cigarette and additional design features such as the addition of menthol to some cigarettes, high and normal tar levels, and high ventilation. Trial batches of cigarettes will be tested for acceptability by test panels of smokers prior to bulk manufacturing. Cigarettes will be packaged in standard packs of 20 cigarettes each that mimic commercial cigarette packaging. Analytical methods have been set up and the various cigarette batches manufactured will be analyzed for nicotine and related minor alkaloids, nicotine yield in smoke condensate, menthol, moisture content, and other factors. Analyses will be performed on an annual basis to monitor the shelf life of these batches during distribution and use by investigators.
Conclusions: Cigarettes will be distributed to researchers as approved by NIDA.
Financial Support: NIDA contract HHSN271201000003C

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ESCITALOPRAM ATTENUATES MODAFINIL'S THERAPEUTIC ACTION IN COCAINE-DEPENDENT VOLUNTEERS.

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Aims: Modafinil is a promising pharmacotherapy for cocaine dependence. Preclinical data indicate that medications that increase brain 5-HT levels reduce the behavioral effects of stimulants. Therefore, we hypothesized that combining modafinil with an SSRI would improve modafinil's therapeutic efficacy for cocaine dependence.
Methods: This ongoing study is a placebo-controlled, double-blind, parallel-groups evaluation of the effects of treatment with modafinil (0 or 200 mg) alone and in combination with the SSRI escitalopram (0 or 20 mg) on the subjective and reinforcing effects produced by cocaine (0 and 20 mg, IV) in the laboratory. Subjective effects are measured using visual analogue scales and reinforcing effects are measured using choice procedures.
Results: Treatment groups include: Placebo (PLB), Modafinil (MOD), Escitalopram (ESC), and Escitalopram+Modafinil (MOD+ESC). To date, the N=6-8/group with a target N of 16/group. Participants are primarily African American males who are ~43 years of age, who reported using cocaine for ~20 years, and used cocaine ~18 out of the last 30 days. Preliminary analyses revealed that the MOD group exhibited reduced cocaine-induced "High", "Desire", "Likely to Use", and choices for cocaine during self-administration. Interestingly, these effects were abolished in the MOD+ESC group.
Conclusions: Consistent with previous studies, our results indicate that modafinil attenuates the subjective and reinforcing effects produced by cocaine in the laboratory. The reversal of effects seen in the MOD+ESC group suggests that increased 5-HT did not interfere with cocaine's subjective and reinforcing effects as predicted, but rather reduced modafinil's therapeutic effects. By inference, this study reveals the importance of the DAT in the effects produced by modafinil. We hypothesize that the use of a combination pharmacotherapeutic approach allowed for determination of the mechanism of action for an already promising candidate compound. In addition, evaluating evidence-based drug combinations offers the possibility of discovering drug synergism.
Financial Support: 1RC1DA028387

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SELF-REPORTS OF HEROIN USERS WHO CONTINUE TO USE HEROIN AFTER TAKING NALTREXONE FOR EXTENDED-RELEASE (VIVITROL®): A PILOT STUDY.

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Aims: Since laboratory studies show that naltrexone provides excellent blockade of the effects of opiates, using heroin while under naltrexone blockade should not be reinforcing. Yet some individuals repeatedly use heroin despite adhering to a prescription of naltrexone for extended release injectable suspension (XR-NTX). We sought to understand this counterintuitive drug-taking by investigating self-reports of participants' experiences in taking heroin while under XR-NTX blockade.
Methods: Participants in a randomized controlled trial of employment-based reinforcement of XR-NTX adherence (N=38) who took XR-NTX and who tested positive for heroin during the previous week were asked how high they felt and how much heroin they used, whether they used cocaine concurrently, and routes of administration. In total, 17 participants completed 106 questionnaires. For comparison, 14 questionnaires were given to 3 participants who did not take XR-NTX, but who tested positive for heroin.
Results: Participants who took heroin while under naltrexone blockade reported no effect of heroin (0 rating of high on a 0 to 10 scale) on 81 of 106 questionnaires (76%). In contrast, participants who took heroin when not blocked by naltrexone always reported an effect of heroin. Cocaine was used with heroin in 61% of cases, but the route of administration was the same in only 23% of cases of concurrent use. Cases of use under blockade increased each week of the 4-week inter-dose interval; 21% of incidents occurred in the first week, compared to 32% in the last week.
Conclusions: XR-NTX appears to have blocked the subjective effects of heroin in most cases. Cocaine may be involved in compromising the effectiveness of XR-NTX in reducing heroin use, but combined use of heroin and cocaine in a single administration does not account for much of the heroin use in this study. Heroin use may be more likely later in the inter-dose interval, when blood levels of XR-NTX are lowest. Further investigation is required.
Financial Support: NIDA R01DA019497, Vivitrol® supplied by Alkermes at no cost.

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DRUG USE IN RURAL CHINA.

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Aims: We conducted a preliminary investigation to explore drug abuse patterns in rural areas and to compare characteristics of drug users from urban and rural areas of Hunan province, China.
Methods: Data collected by local public security bureau between 2005 and 2008 on 1639 newly registered drug abusers in 5 urban areas (n=812 in 2.5 million population) and 5 rural areas (n=827 in 4.5 million population) of Hunan Province was analyzed.
Results: Rural and urban drug users were generally comparable with regard to gender (84% male); age (98% ages 19-47 years, range 14-60 years); education (82% had ≤9 years of school); and marital status (30% single). Heroin was the main abused drug (81% of rural vs. 74% urban, $p<0.01$), followed by ketamine (12% rural vs. 15% urban, $p<0.01$); 39% reported lifetime injection drug use (no significant difference between rural and urban); 27 individuals (2%) reported being HIV positive. Drug users from the rural areas were younger (31 vs. 34, $p<0.001$), started drug use earlier (27 vs. 30, $p<0.001$), spent less money on drugs in the past month ($160 vs. $235 equivalent, $p<0.001$), and reported lower rates of crime or criminal records (19% vs. 30%, $p<0.001$).
Conclusions: The numbers of newly registered drug users from urban and rural areas were comparable, despite a substantially larger population base in rural areas. Despite having similar durations of drug use prior to registration, rural users were younger, had an earlier age of onset of drug use, spent less money on drugs, and had less extensive criminal histories. More detailed studies are needed to further investigate potential differences between drug use prevalence and patterns in rural and urban areas of China.
Financial Support: the "Eleventh Five-year"National Science & Technology Pillar Program 2006BAK09B08

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PROPERTIES OF DSM DISORDERED GAMBLING CRITERIA IN FRENCH GAMBLERS.

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Aims: The DSM-V work group proposed to include disordered gambling within the current Substance-related disorders that would be renamed. Proposed criteria still have to be examined.
Objective: To assess some psychometric properties and to discuss the classification of disordered gambling criteria in gamblers seeking a treatment for at least one addiction in outpatient addiction clinic settings.
Methods: Gamblers were defined as either disordered gamblers or non-disordered gamblers following several classification methods: a) DSM-IV criteria for pathological gambling, b) DSM-IV criteria for pathological gambling adapted from substance-related disorders criteria, c) DSM-V proposed criteria, d) South Oaks Gambling Scale score higher than 5. Reliability (Cronbach's alpha), validity (Phi, Discriminant function analyses, correlations, multivariate regression models) and diagnosis accuracy (Kappa coefficients) were assessed for each classification method.
Results: Among 228 gamblers, prevalence of disordered gambling ranged from 24.7% to 34.1% according to the used classification. All the criteria were found to exhibit satisfactory reliability (Cronbach's alpha ranged from .89 to .92) and validity. However, some criteria had higher discriminative properties than others. The classification accuracy seemed to be similar regardless of the methods used (Kappa ranged from .69 to .94).
Conclusions: Disordered gambling might be assessed using same criteria used for substance-related disorders. Proposed DSM-V criteria seemed not to alter diagnosis accuracy. Using weighted criteria might be useful to assess the severity of disordered gambling.
Financial Support: PRA-CNRS (2009-2011) to M. Fatséas
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WITHDRAWN

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IMPACT OF RECOVERY MANAGEMENT CHECKUPS ON HIV-POSITIVE SUBSTANCE USERS OVER 4 YEARS.

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Aims: This experiment tests the effectiveness of quarterly Recovery Management Checkups (RMC) over 4 years with HIV-positive substance users.
Methods: Participants were 61 HIV positive substance users who were 61% Male, 84% African American, 70% age 30-49, 91% with dependence, 63% with co-occurring psychiatric problems, and 46% with moderate to high levels of crime and violence. Participants were randomly assigned to either the RMC or control condition 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; linkage to treatment, 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. 51%, OR=2.24), return to treatment sooner (44 v 11 months, d=0.74), return to treatment more times (1.9 vs. 0.9 times, d=0.72), receive more treatment (112 vs. 79 days, d=0.23), have fewer successive quarter in the community using (5.3 vs. 6.8, d=-0.27), lower average substance frequency scales (.06 vs. .12 SFS, d=-0.59), have fewer substance problems per month (3.4 vs. 7.5 problems, d=-0.49), and reported more total days of abstinence (1166 vs.952 days, d=0.56). Lower SFS scores were in turn associated with lower average HIV risk behavior scale scores.
Conclusions: RMC is an effective method of monitoring and re-intervening with chronic substance users who are HIV positive and is associated with better long-term outcomes. While RMC increased the likelihood of entering treatment and improving outcomes, each time a person relapsed and used it again RMC was less effective – suggesting the importance of doing it well the first time.
Financial Support: The National Institute on Drug Abuse Grant number R37 DA11323.

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CHILDHOOD ADHD AND ADULT MARIJUANA USE.

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Aims: Many studies have documented that individuals with ADHD are at risk for increased substance use/abuse (Iacono et al., 2008; Zucker, 2006). However, the specificity of the link between childhood ADHD and later marijuana (MJ) use remains unclear. The present study examines the link between childhood symptoms of ADHD and ODD and MJ use in adulthood. Based upon previous work suggesting that childhood ADHD and conduct problems predict adolescent MJ use (MacLean et al., 2008), it is hypothesized that childhood ADHD and ODD will predict MJ use in adulthood.
Methods: Participants were 364 adults (ages 19-33) recruited from a large pool of individuals diagnosed as children with ADHD-age at initial evaluation: 5-16 years. A control group consisted of 240 adults without ADHD matched on age, gender, and race. Adult MJ use was assessed through interview.
Results: Group comparisons were conducted to investigate adult differences in MJ use. Initiation of use was not significant across groups (X2=.68, ns); as many control individuals had tried MJ as individuals with childhood ADHD. However, among those who had tried MJ, individuals with childhood ADHD were using with more frequency than controls during the past 3 months (F=4.42, p<.05), and past 12 months (F=3.42, p<.07). Among individuals with ADHD, regression analyses were conducted using childhood symptoms of inattention, impulsivity/hyperactivity, and ODD to predict adult MJ use. Symptoms of ODD predicted initiation of use (B=.37, p<.05), use in past 6 years (B=1.46, p<.05), and time since last use of MJ (B=-.42, p<.05) above and beyond symptoms of ADHD.
Conclusions: Although age-normative MJ use may mask initiation differences, those with childhood ADHD have more frequent MJ use in adulthood. Among those with childhood ADHD, those with comorbid ODD symptoms are at increased risk for pervasive MJ use in adulthood.
Financial Support: This research was supported by Grants from NIAAA, NIDA, NIMH, and NIEHS.

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INTRANASAL DRUG USE AS A COMPONENT IN "COMBINED" PREVENTION OF HEPATITIS C VIRUS TRANSMISSION AMONG INJECTING DRUG USERS: NEW YORK CITY, 2005 – 2010.

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Aims: HIV and hepatitis C virus (HCV) are transmitted through multi-person use of drug injection equipment. Implementation of combined HIV prevention programs, including large-scale syringe exchange, was followed by a large decrease in HIV incidence among injecting drug users (IDUs) in New York City. Here we examine HCV prevalence among IDUs in the combined program environment, and the potential role of intranasal heroin use in reducing HCV acquisition.
Methods: 726 injecting drug users were recruited from 2005 – 2010 at a large drug detoxification program in New York City. A structured interview was administered and serum samples were collected for HIV and HCV testing. HCV prevalence and risk behaviors were compared to prevalence and risk behaviors among IDUs recruited from the same program in 1990-1991.
Results: Prevalence was 71% among the 2005-10 subjects and 91% among the 1990-91 subjects (p > .001). In a multiple logistic regression analysis, HCV seropositivity among 2005 – 2010 subjects was positively associated with more years injecting, Latino ethnicity, previous testing for HCV, and recent injection of speedball, and negatively associated with recent intranasal use of heroin and speedball. Comparison with the 1990-91 samples showed less passing on of used syringes among 2005-2010 HCV seropositive subjects.
Conclusions: Implementation of "combined" HIV prevention programs, including large-scale syringe exchange, may reduce HCV seroprevalence among IDUs through a mechanism of reducing transmission behavior. Encouraging intranasal use as an alternative to injection among current IDUs may be a viable new strategy for reducing HCV transmission.
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NALOXONE-INDUCED TASTE AVERSIONS IN OPIATE-NAïVE F344 AND LEW RAT STRAINS.

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Aims: Although morphine differentially induces taste aversions in the inbred F344 and LEW rat strains (F344 > LEW), the basis for these differences is unknown. One possibility is that the strains differ in basal opioid tone that mediates the differential reactivity to morphine, e.g., differential receptivity to agonists vs. antagonists. The present study addressed this by examining the ability of the opioid antagonist naloxone to induce taste aversions in F344 and LEW rats.
Methods: In two experiments, opioid naïve, male F344 and LEW rats were given access to a novel saccharin solution (20 min) followed by IP injections of naloxone (0, 3.2, 5.6 and 10; Experiment 1 or 0, 10, 18 and 32 mg/kg; Experiment 2). These pairings were given every 4th day for a total of four pairings with intervening water recovery sessions. A final aversion test followed this conditioning.
Results: A 2 x 4 mixed-model ANOVA on the final aversion test in Experiment 1 revealed no significant main effects or interaction. All subjects drank saccharin at high levels. A similar analysis in Experiment 2 revealed significant effects of Strain and Dose as well as a significant Strain x Dose interaction. LEW subjects injected with 18 and 32 mg/kg naloxone drank less than controls (0 mg/kg). Those injected with 32 mg/kg drank less than those injected with 10 mg/kg. There were no differences among the F344 subjects injected with naloxone, and none drank less than controls. At 32 mg/kg naloxone, LEW subjects drank less than F344 subjects.
Conclusions: The differential ability of naloxone to induce taste aversions in LEW and F344 rats (LEW > F344) is opposite to the effects of morphine in these strains (F344 > LEW). These data suggest that the differential reactivity to morphine in F344 rats may be a function of differences in basal tone that increase sensitivity to agonists in this strain (and decrease its sensitivity to antagonists). Conversely, the lack of sensitivity of the LEW strain to morphine appears to be a function of its differential (increased) sensitivity to the antagonist.
Financial Support: This work was supported by a grant from the Mellon Foundation to ALR.

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MDMA (ECSTASY) USE IS ASSOCIATED WITH LASTING INCREASES IN CORTICAL 5-HT2A RECEPTORS.

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Aims: MDMA is a popular recreational drug that produces loss of cortical serotonin (5-HT) axons in animal models. Whether MDMA produces 5-HT axon loss in humans remains controversial. The 5-HT2A receptor is post-synaptic to 5-HT axons in cortex and upregulates in the absence of agonist signaling. Thus, cortical 5-HT2A receptor status can serve as an assay of pre-synaptic 5-HT neurotransmission. Our primary hypothesis was that MDMA users would have increased 5-HT2A receptor levels in cortex, relative to control subjects—a result consistent with 5-HT axon loss and concomitant reductions in 5-HT release.
Methods: We studied 25 MDMA users abstinent for at least 90 days (mean 528.64 days) and 10 non-MDMA users. Cortical 5-HT2A receptor levels were measured using PET and the radioligand [18F]setoperone. The cerebellum was used as a reference region for determining receptor binding potential (a surrogate for receptor level). We used corrected statistical thresholds and standard analysis methods as implemented in SPM5.
Results: MDMA users had greater binding potential than control subjects in the posterior cortex, with peak differences in the right occipital cortex (t-test). Within the MDMA user group, greater lifetime MDMA use was significantly positively correlated with increased 5-HT2A receptor binding potential in the right lingual, right fusiform, left angular, left precentral, and right frontal superior gyri (linear regression). In contrast, there were no brain regions in which MDMA use was associated with lower 5-HT2A receptor levels.
Conclusions: MDMA use was associated with increased 5-HT2A receptor levels, a finding consistent with MDMA-induced loss of 5-HT axons and subsequent reductions in 5-HT agonist signaling, leading to compensatory upregulation of the 5-HT2A receptor. This finding, in long-abstinent MDMA users, suggests strongly that MDMA produces 5-HT axon loss in humans, similar to that demonstrated in animal models.
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BREAKDOWNS IN CONSCIOUS AND UNCONSCIOUS CONTROL IN OPIATE ADDICTION.

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Aims: Drug behavior is initiated by a conscious system and maintained by an unconscious system (Everitt et al., 2008). Both drug addiction and relapse result from a loss of control over an impulsive response. However, it is unclear whether this impulsive responding results from a disruption in conscious or unconscious control.
Using a response inhibition task, we tested whether patients with substance abuse disorder would exhibit a decline in control. Since our patients were long-term opiate abusers, we hypothesized that both their conscious and unconscious control would be impaired.
Methods: 41 opiate-abusers in the detoxification unit being treated with methadone doses tapering from 25 mg to 5 mg. Participants were presented with two arrows, one after the other. The arrows could either point in the same direction or point in opposite directions. Participants responded by pressing a key to indicate the direction of the second arrow. Participants completed 2 blocks where either the 1st arrow was visible (conscious control) or the 1st arrow was masked so that participants were unaware of its presentation (unconscious control).
Results: In opiate addicts, both conscious and unconscious control were dramatically impaired. This finding didn't result in simple slowing of reaction times or more errors. While 95% of control participants showed both conscious and unconscious control, only 19% of patients exerted both conscious and unconscious control, $\chi 2$ df(1) = 22.56, p < .00001. Moreover, a numerically greater percentage of opiate patients showed no control (21%) than those patients showing both conscious and unconscious control (19%).
Conclusions: Both conscious and unconscious control are impaired in patients with opiate addiction. Both the initial addiction and relapse in opiate addiction likely results from both conscious and unconscious control deficits implicating both prefrontal and striatum dysfunctions.
Financial Support: This work was supported by grants from The College of the Holy Cross to GJD, and an NIH grant (5R01DA027138-02) to GG and GJD.

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DEVELOPMENT OF A NEW DRUM THERAPY TREATMENT PROTOCOL FOR AMERICAN INDIANS/ALASKA NATIVES WITH SUBSTANCE USE DISORDERS.

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Aims: To develop the preliminary treatment protocol of Drum-Assisted Recovery Therapy for Native Americans (DARTNA), a new drum therapy substance abuse treatment protocol for American Indians/Alaska Natives (AI/ANs) with substance use disorders. The development of DARTNA will assist towards developing a drum therapy treatment protocol in a culturally-relevant manner for AI/ANs.
Methods: Three focus groups among: nine AI/AN substance abuse counselors, four Community Advisory Board members, and six AI/ANs with current or past substance use disorders were conducted to obtain feedback on DARTNA prior to pilot testing. The discussions, held at United American Indian Involvement, Inc. (UAII) in Los Angeles, CA were audio-recorded, transcribed, and analyzed using ATLAS.ti.
Results: Findings from the focus groups were in general favor with regards to the utilization of drumming alongside 12-steps of Alcoholics Anonymous and, concepts of the American Indian Medicine Wheel delivered within a 12-week outpatient treatment format. Several major themes emerged across the three focus groups, including tribal diversity in terms of traditions associated with drumming and the need to acknowledge both the differences and the similarities (e.g., respect for the drum, healing aspects), importance of the drum therapy leaders (e.g., well-respected traditional leaders in the community and counselors), role of women (e.g., usually not drumming, rather accompanying via singing and dancing), drumming as sacred (e.g., focus on traditional and cultural relevance rather than simply a musical activity), and logistical issues (e.g., scheduling sessions twice rather than three times a week).
Conclusions: These results substantiate general community acceptance of a culturally-relevant substance abuse treatment approach utilizing drumming within the general framework of an American Indian/Alaska Native clinic serving this population within an urban environment.
Financial Support: NIH/NCCAM 1R21AT005360-01A1

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EXERCISE AND NUTRITION PROFILES IN PATIENTS WITH SUBSTANCE USE DISORDERS.

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Aims: Traditional therapies for substance use disorders (SUDs) are often acute interventions focused on treating withdrawal symptoms and encouraging abstinence from substance use; long-term relapse rates in patients with SUDs remain high. Exercise affects physical and psychological well-being, and used as adjunct treatment, may help encourage long-term abstinence from substance use. In clinical studies, exercise increases abstinence rates, and decreases cravings and withdrawal symptoms in tobacco smokers, alcohol and polydrug users, and cocaine addicts. While data about the efficacy of exercise as adjunct to standard therapy in patients with SUDs appear promising, its effectiveness also depends on acceptability to the target population. Little is known about these patients' willingness to adopt healthy lifestyles as an adjunct to standard SUD treatment. This research identified attitudes toward and knowledge about exercise and nutrition as well as current practices in substance abusers.
Methods: 205 people with a history of SUDs completed a computerized survey using an interactive program on a laptop computer at the inpatient or outpatient facility where they were receiving treatment. Demographic, substance use, nutrition and exercise variables were examined.
Results: Subjects were middle-aged (42/9), African-American (58%) and Caucasian (37%), women (48%) and men (52%) in inpatient (61%) and outpatient (39%) treatment programs. Men primarily abused alcohol; women abused alcohol and cocaine. Inpatient subjects reported eating significantly better (prior to admission) than outpatients and men exhibited more exercise knowledge and reported better compliance with recommended exercise levels than women. While knowledge about exercise and nutrition guidelines was low, subjects thought healthy lifestyles could positively impact their SUD recovery.
Conclusions: Clearly, patients with SUDs believe that nutrition and exercise are important to their recovery efforts and interventions that focus on overall health in these patients potentially provide a unique opportunity to affect substance use behavior.
Financial Support: VCU IWH Seed Grant

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SPIKING BRAIN COCAINE LEVELS AND THE IMPLICATIONS FOR A MODEL OF ADDICTION.

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Aims: In order to understand the neurobiology underlying addiction there is a need for an animal model which encompasses symptoms such as escalation of drug use and increased motivation to take drug. This is typically studied using extended access models that maintain constant blood levels of cocaine. By contrast, here we examined the effects of repeatedly spiking cocaine levels throughout the course of the day on producing an "addicted" phenotype in the rat.
Methods: Male, Sprague-Dawley rats implanted with IV catheters were given 3 hours daily access, where the animal was able to pick its preferred dose and speed of injection, until they were capable of consistently titrating their brain cocaine levels (usually 1-3 days), followed by 21 days of 24 hours/day self-administration (5/55: 5 min lever access followed by a 55 min timeout, which causes a spike in brain cocaine levels followed by a decay during the timeout). Progressive ratio dose response curves (0.3 – 1.7 mg/kg) and reinstatement responding after 10 days of deprivation were also assessed and compared to rats receiving 2 hours daily access.
Results: After 21 days of 5/55 we observed a 100% escalation in intake. Preferred dose and speed of injection also increased over time. Preferred dose increases by 60% from week 1 to week 3 (week one preferred dose 2.2 mg/kg ± 0.29, week two preferred dose 3.5 mg/kg ± 0.56). 5/55 rats also showed an increase in peak preferred dose on the PR dose response curve and dramatically increased reinstatement responding as compared to 2 hr rats (5/55: 214 ± 26.2, 2 hr: 59.3 ± 12.6).
Conclusions: Self-administration conditions that produce repeated spikes in cocaine levels produce an addictive phenotype as observed by escalation in intake, increased motivation to obtain cocaine and increased susceptibility to relapse. Thus it appears that spiking of cocaine levels is sufficient in driving the addiction process while the maintenance of blood levels in not necessary.
Financial Support: F31 DA025443 (CVD) and R01 DA14030 (DCSR)

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CORRELATES OF HAART USE AMONG HOSPITALIZED HIV-INFECTED CRACK COCAINE USERS.

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Aims: HIV-infected crack cocaine users have poor engagement in HIV primary care services and low use of antiretroviral therapy. We examined correlates of HAART use in this population.
Methods: 413 HIV-infected crack cocaine users hospitalized at Grady Memorial Hospital, Atlanta, GA, and Jackson Memorial Hospital, Miami, FL, were enrolled in Project HOPE, a randomized trial of a behavioral intervention that seeks to improve linkage to HIV primary care. We conducted a cross-sectional analysis of the baseline data for those participants who had any lifetime use of HAART or CD4 ≤ 350. Multivariate logistic regression was performed to evaluate correlates of current HAART use.
Results: Among 358 eligible participants, mean age was 45 years, 51% were women, and 90% were African-American. Median CD4 count was 149 cells/uL. Despite being eligible for HAART according to DHHS guidelines, only 33% were currently on HAART. Correlates of HAART use in the multivariate analysis were at least 2 visits to HIV care in the past 6 months (AOR 5.87; 95% CI 3.06, 11.26), drug treatment in the past 6 months (AOR 2.83; 95% CI 1.28, 6.24) and a strong patient-provider relationship (AOR 2.68; 95% CI 1.36, 5.25). Current homelessness was negatively associated with use of HAART (AOR 0.40; 95% CI 0.19, 0.84). No drug use variables were independently associated with HAART utilization. Among those on HAART, median viral load was 3,280 copies/ml, and 33% had viral load < 400 copies/ml.
Conclusions: Among hospitalized HIV-infected crack cocaine users, only 1/3 of eligible individuals were using HAART, and of these, only 1/3 had an undetectable viral load. This suggests that interpersonal and structural factors may be as important as individual factors when examining barriers to effective HAART use among cocaine users. Despite use of HAART, many remain capable of HIV transmission with potentially resistant virus.
Financial Support: NIDA/NIH

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SEX DIFFERENCES IN COCAINE REINFORCEMENT AND REINSTATEMENT VARY WITH STAGE OF ADDICTION.

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Aims: The majority of behavioral studies on cocaine addiction have been performed in males following short access (ShA) exposure to the drug. Much less is known using extended access (ExA) paradigms that model later stages of addiction, and regarding differences between males and females. The purpose of this study was to examine sex differences following ShA versus ExA cocaine self-administration on subsequent cocaine-taking and seeking behaviors.
Methods: Adult male (n=36) and female (n=32) Sprague-Dawley rats were trained to self-administer cocaine (1.5 mg/kg/infusion, 20 infusion max) under a fixed ratio 1 schedule. 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 consisting of 10 days of 24h access to cocaine infusions under a discrete trial procedure (4 infusions/hr). Following 14 days of abstinence, rats were tested under a progressive ratio (PR) schedule (0.5 mg/kg/infusion), or under a within-session extinction/cue-induced reinstatement paradigm.
Results: We found PR responding for cocaine to be significantly higher in females than males after ExA self-administration, while no sex differences were observed after ShA cocaine self-administration. Reinstatement responding was also significantly higher in ExA compared to ShA animals, and was greater in ShA females than ShA males.
Conclusions: These results indicate that sex differences in both cocaine reinforcement and reinstatement vary according to addiction stage; Females demonstrate a greater sensitivity than males to drug related cues following ShA exposure to drug, and an enhanced motivation for drug in later stages of the addiction process.
Financial Support: Supported by NIDA grant R01DA024716 (WJL)

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THE EFFECTIVENESS OF PSYCHOSOCIAL INTERVENTION FOR HEROIN DEPENDENCE IN MMT IN SHANGHAI.

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Aims: The service currently delivering in MMT clinics is only daily methadone dispense. The comprehensive services have not been incorporated into MMT clinics. In this study, we developed the psychosocial Intervention program and to test its effectiveness in reducing drop out rate and improving psychological status of MMT clients.
Methods: Total of 157 patients were recruited from 2 MMT clinics in Shanghai. 79 patients were randomized assigned to experimental group, 78 patients were assigned to control group. Patients in experimental group received psychosocial intervention, including individual counseling (twice a week); group counseling (Once a month); family therapy (once a month), while patients in control group received usual MMT care. Addiction Severity Index (ASI), HIV/HCV Knowledge scales BDI etc. were used to measure the drug use severity and psychosocial status at baseline and 6-month follow-up interviews.
Results: Some important issues indicated in this study. 1) Both experimental and control groups have problems on employment; 2) HCV infection rate is pretty high, and HCV and AIDS knowledge level are very low in this population; 3) Compare to the control group, the retention rate was significant higher in the experimental group; 4) Other Psychosocial factors, including depression, stigma, and self-esteem should be targeted in the future study.
Conclusions: Comprehensive psychosocial intervention improved retention rate and HIV/HCV related knowledge level among drug users in MMT clinics. But patients still have other psychosocial issues need to be addressed.
Financial Support: Shanghai Hospital Develop Center (SHDC12007223)

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RANK-ORDERING PRESCRIBERS BY OPIOID ABUSE AND DIVERSION RISK.

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Aims: Given the public health burden from abuse of prescription opioids, it is important to develop models that identify prescribers with questionable prescribing behaviors who might contribute to availability of these drugs for abuse. The goal is to develop a model using anonymous unique recipient of dispensed drug data (URDD) that can determine risk trends and inform the development and targeting of Risk Evaluation and Mitigation Strategies (REMS).
Methods: Modeling starts with development of potential concern metrics; eg, opioid abuse is correlated with URDDs procuring opioid prescriptions from multiple physicians. Next, model-training exemplars are identified from publically-announced cases of problematic opioid prescribing. Finally, a mathematical algorithm integrates prescribing risk metrics into a Composite Concern Index.
Results: Analyses conducted over two years resulted in developing 40+ individual opioid prescribing risk metrics. A genetic algorithm provided the most robust model result. Over time, the models improved from a 33% to 83% inclusion of known problem prescribers (exemplars) ranked in the top 180 scores.
Conclusions: Opioid prescribing behavior models can be used to target REMS-compliant educational interventions to prescribers most likely to benefit and to aggregate prescribing trends at various demographic and geographic levels.
Financial Support: Purdue Pharma L.P.; Principled Strategies; Wolters Kluwer; and Polaris Management Partners

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RECOMMENDATIONS ON NATIONAL DRUGGED DRIVING POLICIES SUBMITTED TO THE OFFICE OF NATIONAL DRUG CONTROL POLICY.

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Aims: The fourth National Roadside Survey (2009) of 6,553 weekend nighttime drivers produced a dramatic result: based on the analysis of the oral fluid data, more nighttime drivers (16.3%) were using drugs than were using alcohol (12.4%). A national study by NHTSA (2010) confirmed the prevalence of drugged driving by showing that in 2009 33% of fatally injured drivers tested positive for drugs other than alcohol. The 2010 National Drug Control Strategy released by the White House Office of National Drug Control Policy (ONDCP) called for reducing drugged driving as a major priority. In connection with that effort, the Institute for Behavior and Health (IBH) assembled a broadly-based group of experts to suggest policy recommendations to ONDCP and a research agenda to the National Institute on Drug Abuse (NIDA) on drugged driving. This paper describes the policies and research recommended and the considerations that led to them.
Methods: IBH formed an expert group to develop a White Paper on the status of current drugged driving knowledge and priority research needs for the future. That document formed the basis for six policy recommendations to ONCDP:
Results: The six policy and program areas are designed to:
1. Identify the extent of the drugged driving problem and progress in reducing it;
2. Provide for effective per se drugged driving laws;
3. Establish internal possession laws;
4. Inform the public of the risk of drugged driving;
5. Manage drug- and alcohol-impaired driving offenders;
6. Improve drug- and alcohol-impaired driving enforcement.

Conclusions: This paper describes the policies and research priorities intended to inform and reduce the drugged driving problem in the United States.
Financial Support: ONDCP and NIDA

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THE PREVALENCE OF HIV RISK BEHAVIORS AMONG FELONY DRUG COURT CLIENTS.

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Aims: The high rate of HIV risk behaviors is well documented among incarcerated individuals and has been largely attributed to their high prevalence of drug use. Although some research has indicated similar rates among probationers and parolees living in the community, virtually no data exist on the prevalence of HIV risk behaviors among the growing numbers of drug court participants. This descriptive study examines the prevalence of these behaviors among a sample of felony drug court clients.
Methods: A total of 269 drug court clients completed a survey measuring the extent to which they engaged in drug use and sexual behaviors that increased their risk for HIV infection. Item frequencies were examined, and chi-square and correlation analyses were used to identify differences in rates of engagement in risk behaviors as a function of demographics. Finally, participant zip codes were mapped to the geographic concentration of HIV/AIDS in Philadelphia to identify clients' risk of coming into contact with the virus.
Results: Relatively few drug court clients engaged in HIV drug risk behaviors (e.g., injection drug use, needle sharing); however, almost 2/3 of the sample engaged in high-risk sexual behaviors (e.g., multiple partners, sex without a condom). Higher rates of engagement in risk behaviors were associated with being male, African American, and younger. Finally, 1/3 of clients resided in areas of Philadelphia in which the AIDS epidemic is considered to be generalized.
Conclusions: Results indicated that drug court clients are at high risk for contracting HIV infection and suggest that drug courts may represent an important opportunity to deliver risk reduction interventions, HIV testing, and referral to HIV care. Research should be expanded to further document the prevalence of high risk behaviors and HIV/AIDS in this population and to identify useful strategies for reducing risk.
Financial Support: This research was supported by grant #R01-DA-14566 from the National Institute on Drug Abuse.

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REINFORCING EFFECTS OF NICOTINE 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, subjective, and reinforcing effects of oral nicotine in nicotine non-users.
Methods: Eleven 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 24 subjective effects for two hours after each set of capsules. Discrimination at ascending doses of nicotine was tested. Following significant discrimination acquisition, volunteers were asked to choose which capsule set they would like to receive to investigate the reinforcing effects of nicotine in these volunteers. Significance ($p<.05$, binomial probability distribution) was determined in blocks of 10 sessions for discrimination and choice testing (i.e., >8 out of 10).
Results: All eleven subjects significantly discriminated between nicotine and placebo ($p<.05$). The lowest dose that was discriminated varied between 1.0-4.0 mg/70kg across volunteers. During choice sessions, six volunteers significantly chose nicotine, while five volunteers significantly chose placebo ($p<.05$). Volunteers that chose nicotine generally reported positive effects of nicotine (e.g., Good Effects, Stimulated), while those that chose placebo (i.e., avoided nicotine) generally reported negative effects of nicotine (e.g., Bad Effects, Lightheaded/Dizzy).
Conclusions: All volunteers significantly acquired oral nicotine discrimination. Six volunteers reliably chose nicotine during the choice sessions, indicating significant reinforcing effects of nicotine. A better understanding of the subjective and reinforcing 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: DA03890

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EMPLOYMENT-BASED REINFORCEMENT OF ADHERENCE TO ORAL NALTREXONE TREATMENT WITHIN UNEMPLOYED INJECTION DRUG USERS: 12-MONTH FOLLOW-UP.

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Aims: Naltrexone is an opioid antagonist that blocks the effects of opioids, but rates of adherence are notoriously poor. Employment-based reinforcement of oral naltrexone administration greatly increases adherence relative to the provision of the medication at no cost, but whether naltrexone use is maintained after discontinuation of the intervention is unknown.
Methods: Recently-detoxified opioid dependent injection drug users were inducted onto oral naltrexone and then randomly assigned to a Contingency (n=35) or Prescription (n=32) group. All participants could attend a model workplace that provided access to paid job skills training and take oral naltrexone for 6 months. Participants in the Contingency group were required to ingest oral naltrexone thrice weekly to enter the workplace. Prescription participants received a take-home prescription and could work independent of naltrexone ingestion. Monthly urine samples were collected and screened for opiates, cocaine, and naltrexone
Results: The Contingency group provided significantly more naltrexone-positive samples during the intervention compared to the Prescription group (72% and 21%, $p<.001$). At the 12-month follow-up, none of the study participants reported taking naltrexone in the past 30 days; there were no group differences in opiate (46% and 43%) and cocaine (50% and 52%) negative samples; and only 18% and 22% of participants reported receiving any substance abuse treatment in the 30 days prior to the assessment, respectively.
Conclusions: Despite high levels of naltrexone adherence in the Contingency group during the 6-month intervention period, adherence did not persist after reinforcement was discontinued. Reinforcement may be required to maintain naltrexone adherence in many injection drug users. Employment-based reinforcement may be an ideal method for arranging naltrexone adherence over extended periods of time.
Financial Support: NIDA R01-DA019386 and T32-DA007209

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VARIABILITY IN SELF-ESTEEM AS A PREDICTOR OF RISKY SEXUAL ATTITUDES IN A COMMUNITY SAMPLE OF FEMALE AFRICAN AMERICAN DRUG USERS.

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Aims: Feelings of self-worth have been shown to buffer individuals against drug use and HIV-related risk behaviors. However, how consistently individuals maintain positive self-related attitudes and for whom these attitudes may be most beneficial, is less clear. The purpose of the current study was to investigate how variability in self-esteem was associated with female African American drug users' attitudes about engaging in risky sexual behaviors.
Methods: Data for this study were collected from a community sample of 105 African American women living near a metropolitan area of Kentucky at three time points (intake, 6, and 12-month follow-up). Participants had a mean age of 33.9 years. A majority reported being unmarried (92%) and having children (65%). Approximately 54% were employed either full or part-time. Eighty-one percent of participants reported making less than $20,000 in the past year.
Results: Results of a series of multiple linear regression models revealed that variability/instabilty in female African American drug users' self-esteem (i.e., computed as the standard deviation across all 3 waves) was associated with needing to be in a risky sexual relationship to feel good about one's self ($B = .19$, $p<.01$), believing that a partner is safe by the way he looks ($B = .16$, $p<.05$), and feeling at greater risk for HIV infection ($B = .17$, $p<.01$). Greater variability in self-esteem was also associated with lower levels of relationship power ($B = -.13$, $p = .08$) and less decision-making dominance ($B = -.14$, $p<.05$).
Conclusions: Findings suggest the importance of stable self-worth in promoting healthy decision-making practices in female African American drug users, particularly those involved in risky sexual relationships. Results are discussed in terms of HIV risk, substance abuse treatment needs, and recovery in this population.
Financial Support: This research is funded by the National Institute on Drug Abuse (R01-DA022967, PI: Oser; K01-21309 PI: Oser).

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PRECLINICAL EVALUATION OF GZ-793A AS A PHARMACOTHERAPY FOR METHAMPHETAMINE ABUSE.

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Aims: Methamphetamine (METH) interacts with the vesicular monoamine transporter-2 (VMAT2) to increase extracellular dopamine (DA) leading to reward and abuse. We hypothesize that a potent and selective VMAT2 inhibitor (GZ-793A) will decrease the METH-evoked DA release from striatal synaptic vesicles and slices to decrease METH-induced reward.
Methods: DA uptake, DA release and DA content experiments were conducted in rat striatal synaptic vesicles and striatal slices. METH self-adminstration, conditioned place preference, and reinstatement experiments were conducted.
Results: In addition to inhibiting DA uptake by VMAT2, GZ-793A increased DA release from synaptic vesicles at two vesicular sites. Tetrabenazine, a VMAT2 inhibitor, blocked GZ-793A-evoked DA release via the high affinity site. GZ-793A decreased METH-evoked DA release from synaptic vesicles in a concentration-dependent manner and this effect was not surmounted by increasing concentrations of METH, indicating a noncompetitive inhibition. Also, GZ-793A inhibited METH-evoked DA release from slices without altering nicotine- or electrically-evoked DA release, indicating its selectivity for inhibiting METH. GZ-793A (s.c.) did not alter striatal tissue or vesicular DA content. Rather than potentiating the METH-induced DA depletion, GZ-793A blocked the METH-induced DA depletion, indicating that it may prevent METH toxicity. In behavioral experiments, GZ-793A specifically decreased METH self-administration; tolerance did not develop to this effect with repeated GZ-793A treatment. GZ-793A also blocked METH conditioned place preference. Alone, GZ-793A did not produce reward and did not substitute for METH in the self-administration assay. GZ-793A also blocked cue-induced reinstatement of METH seeking, suggesting it may be a beneficial treatment for relapse.
Conclusions: Thus, GZ-793A inhibition of the effects of METH at VMAT2 and the GZ-793A-induced decrease in METH reward and reinstatement indicate that GZ-793A is a high value preclinical candidate for advancement as a treatment for METH abuse.
Financial Support: Funding provided by DA13519 and DA016176

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POSITIVE AFFECT IN TREATMENT ONSET CAN HAVE NEGATIVE IMPACT ON LATER OUTCOMES AFTER RESIDENTIAL HEROIN DETOXIFICATION PROGRAM.

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Aims: The aims of this study were to identify whether opiate dependent patients' positive and negative affects can predict the treatment outcome after a residential detoxification program. Our hypothesis is that positive and negative affects are correlated with positive and negative outcome treatment, respectively.
Methods: Participants were 81 male opiate-dependent patients, all heroin hydrochloride smokers before entering to the treatment program. A successful completion of the treatment outcome was defined as retention for all three urine tests conducted in the following three months after four weeks treatment completion. After a complete clinical assessment, affects were measured using a modified version of Positive Affect (PA), such as interested, excited, strong, etc, and Negative Affect (NA), such as upset, guilty, scared, etc, Schedule (PANAS).
Results: 30 patients remained abstinent in three months follow up after completion of four weeks program. The result indicates that four variables predict 3 months retention significantly (degree of freedom=12, Chi-squared=43.1, correct classification rate=0.802, $p<10\text{-}5$). Higher education ($p=0.006$) and number of sexual activity during the last month before treatment entry (LMBT) ($p=0.04$) predicted a positive outcome. In contrast, number of physical disputes during the LMBT ($p=0.005$) and particularly relevant for our aim of study, PA score ($p=0.017$), predicted a negative outcome. In addition, PA score predicted the negative outcome in all three months significantly with retention and abstinence measures.
Conclusions: Our results indicate that self report of positive affect in treatment onset has a significant negative correlation with the treatment outcome. Positive affect may have impacts on treatment outcome through lower acceptance or insight and higher sensation seeking or impulsivity. Clinical and psychological assessment before and during treatment can help to detect special needs and conduct more patient-tailored interventions to improve outcomes.
Financial Support: Tehran University of Medical Sciences

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THE NEUROPHARMACOLOGICAL AND TOXICOLOGICAL EFFECTS OF INHALING A LOCAL EGYPTIAN GLUE.

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Aims: Investigation of the physicochemical properties, neuropharmacological and toxicological effects of inhaling a local glue which is widely abused by street children and other adolescents in Egypt.
Methods: Physicochemical properties and chemical composition of glue by (IR), (1H-NMR) and (GC-MS). Neuropharmacological tests: Effect on Pentobarbital sleeping time, rotarod test for motor coordination and activity cage for locomotor activity. Determination of lipid peroxidation by measuring MDA in cortex and cerebellum and glutamate levels in rat's hippocampus. Toluene was used as a reference inhalant. Three inhaled concentration of glue and toluene were investigated.
Results: "Kolla" contains 15 volatile solvents in different percentages including: toluene, p-xylene, hexane, n-octane and n-ethylbenzene. Single (30 minutes) inhalation of glue (1000 and 4000 ppm) and toluene (5610 and 22576 ppm) prolonged pentobarbital (30 mg/kg, i.p) sleeping time. Higher concentrations of glue (8000 ppm) and toluene (45153 ppm) antagonized pentobarbital hypnotic action. Single inhalation of the tested substances produced motor incoordination and decreased locomotor activity. Toluene (45153 ppm) increased locomotor activity. Repeated inhalation (30 min/day for 10 days) of glue and toluene increased locomotor activity and led to a dose-dependent oxidative stress evidenced by an increase in the level of the lipid peroxidation product (MDA) in cortex and cerebellum. Both inhalants increased levels of glutamate in rats hippocampus. Repeated daily inhalation of 8000 ppm glue leads to mild lobular and portal inflammation, hydropic degeneration and mild fatty changes in rat's liver.
Conclusions: "Kolla" contains at least 15 toxic solvents. Single inhalation of this glue potentiated the hypnotic action of pentobarbital and produced an inhibition of locomotor activity and motor incoordination. Repeated inhalation leads to locomotor hyperactivity, causes oxidative stress and increases levels of the brain neuroexcitatory transmitter "glutamate". Repeated daily inhalation of 8000 ppm glue leads to marked histopathological changes in liver.
Financial Support: None

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PAIN MEDICATION USE AMONG A UNIVERSITY SAMPLE FROM LEBANON: A CLOSER LOOK INTO SOURCES, REASONS, AND POTENTIAL CORRELATES.

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Aims: Pain medications when used non-medically pose significant health problems given their potentially addictive and withdrawal nature. More youth are using these drugs worldwide, yet little is known about their behavior in the Arab region. A cross-sectional study was conducted in Lebanon to investigate patterns of pain medications use as well as possible correlates among a university sample.
Methods: Undergraduate and graduate students (n=573) from the American University of Beirut (AUB) participated in this study (IRB-approved). Selection was undertaken using proportionate cluster sampling. A self-filled anonymous questionnaire was used.
Results: Lifetime and past-year prevalence of students reporting non-medical use of pain medications was 16% and 10%, respectively; proportions were almost two-fold for medical use (37% and 19%, respectively). Diversion was admitted by about 16% of the lifetime medical users. Students who used pain medication non-medically predominantly did so for the drug's therapeutic purpose. Most students reported a family member or a health professional as means to obtain the drug, yet sources varied by motivation to use. Past year non-medical use of pain medications was associated with significantly higher odds of past year alcohol abuse (OR=10.4, 95%CI: 2.3, 47.2), cigarette (OR= 2.5, 95%CI: 1.1, 5.8) and marijuana use (OR= 4.8, 95%CI: 1.9, 12.2), adjusting for demographics.
Conclusions: Non-medical use of pain medications in youth warrants closer attention, given the risk of contraindications and addiction, or even death. Increased awareness about the dangers of non-medical use and diversion is needed at the level of youth and parents. Improved monitoring mechanisms among pharmacists and doctors are important for better control.
Financial Support: American University of Beirut (University Research Board) seed grant

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SEX DIFFERENCES IN THE EFFECTS OF EARLY LIFE STRESS ON ADDICTION-RELATED COGNITIVE DEFICITS.

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Aims: A history of early life stress is an established risk factor for drug addiction. However, the mechanisms by which stress in childhood increases risk for addiction in adulthood are not well defined.
Aims:1) Identify cognitive consequences of child abuse or neglect that represent a risk for drug addiction. 2) Determine if the effects of stress exposure in childhood on decision making or inhibitory control differ between the sexes.
Hypothesis:A history of early life stress is associated with deficits in decision making and inhibitory control which mirror deficits observed in cocaine-dependent individuals and differ for males and females.
Methods: Thirty-seven subjects ages 21-57 underwent an fMRI scan while performing a task of decision making under risk and a stop-signal task. Eleven subjects had histories of child abuse or neglect (ELS; 5 male,6 female), fifteen were healthy controls (CON; 8 male,7 female), and eleven were cocaine-dependent males (COC). ANOVAs and t-tests of behavioral data were performed in SPSS. Image processing and analyses were conducted using SPM5 software.
Results: Significant sex-specific cognitive effects of childhood stress were observed. Both ELS and COC males lacked adaptive slowing behavior following errors relative to CON males. Conversely, ELS females displayed exaggerated slowing following both errors and successful stops. Childhood stress did not alter risk-biased decision making behavior in females, yet both ELS males and COC males made riskier decisions than CON males. Preliminary fMRI results suggest that childhood stress diminishes ventral striatal engagement during decision making in females and the medial frontal gyrus in males.
Conclusions: These findings suggest that the effects of early life stress on decision making and response to errors in males represent a risk phenotype for addiction. Preliminary fMRI results support a sex-specific effect of childhood stress on neural processes involved in decision making. The addition of a female cocaine-dependent sample will allow us to determine if the deficits observed in ELS females contribute to a vulnerability for addiction.
Financial Support: 5R01DA019999-03

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EFFECT OF SINGLE-PROLONGED STRESS, A MODEL OF PTSD, ON ANXIETY AND COCAINE-INDUCED BEHAVIORS.

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Aims: Post-traumatic stress disorder (PTSD) results in symptoms of fear, anxiety, and depression. The occurrence of PTSD is highly comorbid with addiction, suggesting that PTSD may facilitate vulnerability to substance abuse. This study examined the effect of single-prolonged stress (SPS), a rodent model of PTSD, on behavioral activity, anxiety-like behavior, cocaine-induced behavior, and tyrosine hydroxylase levels.
Methods: Adult male Sprague-Dawley rats were exposed to a modified single-prolonged stress paradigm consisting of 2 hours of restraint stress, 20 minutes of group swimming, isoflurane exposure until general anesthesia, and 7 days of isolation. Following isolation or control handling, activity was measured for 24 hours. Anxiety-like behavior was measured with the defensive burying paradigm and elevated plus maze. The effects of SPS on cocaine-induced locomotion, the development of sensitization, and the development of cocaine-conditioned place preference were examined. Tyrosine hydroxylase within the amygdala and nucleus accumbens after SPS or control handling was examined by Western blot.
Results: SPS rats showed increases in duration of burying, shock reactivity, freezing behavior, and height of bedding on the defensive burying test, indicating heightened levels of stress-induced anxiety. Behavior on the elevated plus maze was not different between groups. SPS did not affect cocaine-induced locomotion or the development of sensitization. SPS rats spent less time on the drug paired side of the conditioning chamber than controls, suggesting reduced sensitivity to cocaine reward. SPS significantly decreased levels of tyrosine hydroxylase in the amygdala and nucleus accumbens compared to control rats.
Conclusions: These data suggest that SPS enhances anxiety-like behavior and decreases behavioral activity. SPS also attenuates the development cocaine conditioned reward, which may be mediated by reduced dopaminergic tone. Future studies will examine the effect of SPS on stress-induced reinstatement to cocaine seeking.
Financial Support: Supported by DA09580 (EMU) and T32 DA07237 (EMU/NE)

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THE HYPOCRETIN/OREXIN SYSTEM REGULATES DOPAMINE RESPONSES TO COCAINE.

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Aims: The hypocretins/orexins (HCRT) influence cocaine reinforcement via actions on the mesolimbic dopamine (DA) system. We have previously shown that infusions of the HCRT 1 receptor antagonist, SB-334867, decrease cocaine self-administration. Additionally, in anesthetized rats, SB-334867 attenuates DA responses to cocaine. The current studies used voltammetry in freely moving rats to further examine the extent to which the HCRT system mediates the effects of cocaine on DA signaling.
Methods: Male Sprague-Dawley rats were implanted with a stimulating electrode in the ventral tegmental area (VTA) and a carbon fiber electrode in the nucleus accumbens. DA release was electrically-evoked every 5 min. Following collection of a stable baseline, rats were treated with i.p. infusions of vehicle or SB-334867 (30 mg/kg) and DA signaling was monitored. A subset of rats also received a single injection of cocaine 30 min following SB-334867 or vehicle to examine the extent to which HCRT signaling influences DA responses to cocaine.
Results: Electrical stimulation of the VTA resulted in stable levels of DA release and uptake. Following vehicle treatment, DA release and uptake remained at baseline levels. By comparison, treatment with SB-334867 reduced evoked DA release within 30 min of treatment although no obvious changes in DA uptake were observed. Additional experiments comparing the effects of cocaine in rats pretreated with SB-334867 or vehicle indicate that blockade of HCRT receptors also alters DA responses to cocaine.
Conclusions: The current studies demonstrate that the HCRT system participates in the regulation of DA signaling under baseline conditions and in responses to cocaine. When combined with previous work indicating that HCRT signaling is necessary to support cocaine self-administration, the current results provide additional evidence for the hypothesis that the HCRT system is involved in reward and reinforcement processes through actions on the mesolimbic DA system.
Financial Support: NIDA K01 DA025279 (R.A.E), R01 DA021325 (S.R.J.), P50 DA06634 (D.C.S.R., S.R.J.)

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SEX DIFFERENCES IN TOBACCO SMOKING-INDUCED UPREGULATION OF BETA2-NACHRS.

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Aims: Women are thought to be reinforced by non-nicotine conditioned stimuli that are strongly associated with smoking, while men are more reinforced by nicotine in cigarettes. Women are not as responsive as men to nicotine replacement therapies - the most widely used smoking cessation tools. Nicotine, the primary addictive chemical in tobacco smoke, upregulates the nicotinic acetylcholine receptors (nAChRs) in the brain. Preclinical studies report greater nicotine-induced upregulation of nAChRs in male vs. female rodents compared to same-sex controls; however, this has not been examined in living humans. Presently, we examined sex-differences in beta2-nAChR availability between men and women smokers compared to same-sex nonsmokers.
Methods: Fifty-two men (26 nonsmokers, 34±11 y; 26 smokers, 33±11y) and fifty-eight women (30 nonsmokers, 33±11y; 28 smokers, 35±10 y) participated in one [123I]5IA SPECT and one MRI scans. At baseline, men and women smokers smoked 16±5cigs/d for 14±8y and 18±6cigs/d for 17±10y, respectively. They were helped to quit smoking for ~1wk with contingency management prior to the SPECT scan.
Results: Preliminary analyses revealed significant differences between men and women smokers in beta2-nAChR availability compared to same sex nonsmokers. Specifically, men smokers had significantly higher beta2-nAChR availability in the striatum (16%), cerebellum (16%) and frontal (14%), parietal (13%), anterior cingulate (15%), occipital (17%) and temporal (14%) cortices compared to men nonsmokers; however, women smokers did not differ significantly from women nonsmokers in striatum (2%), cerebellum (1%) or frontal (1%), parietal (3%) anterior cingulate (6%), occipital (8%) and temporal (4%) cortices.
Conclusions: Sex differences in the upregulation of beta2-nAChRs may explain in part why women have a harder time quitting smoking than men. These preliminary findings suggest the regulatory effect of nicotine on beta2-nAChRs differs significantly between men and women.
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DRUG USE RELAPSE AFTER FIRST TREATMENT AMONG EMERGING ADULTS.

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Aims: Among the few substance-using emerging adults who receive care, sustained recovery is made more challenging by a variety of factors unique to this age group yet commitment to a healthy adult lifestyle at this stage can have substantial lifelong benefits. Little is known about factors that impact drug use relapse after treatment among emerging adults.
Methods: Analyses used data on 1,655 adults pooled from five longitudinal studies conducted in California that collected information using the Natural History Instrument. We compared 396 (24%) adults who initiated first drug treatment during emerging adulthood (age 18-25) to 1,259 (76%) who initiated treatment during later developmental stages (age >26), examining participant characteristics and patterns of drug use and other behaviors over the subsequent 10 years.
Results: Compared to individuals who experienced first treatment during later developmental stages, the emerging adult group included more women (43% vs. 26%); more Whites (42% vs. 32%) and Hispanics (31% vs. 27%) and fewer African Americans (22% vs. 38%); and fewer cocaine (23% vs. 41%) and heroin (24% vs. 30%) users and more methamphetamine (42% vs. 21%) users. Mean (SD) age was 22 (2.1) among emerging adults and 34 (6.1) among older adults. Over 10 years, emerging adults reported more mean months of drug use (35 vs. 32) and incarceration (13 vs. 7) and fewer mean months of employment (31 vs. 44). The two groups had similar drug use relapse rates (about 68%) one year after first treatment. The percentage that used drugs declined for both groups over 10 years, however a significant divergence in use appeared in later years of the observation period, with more emerging adults reporting drug use. Ten-year substance use trajectories will be examined.
Conclusions: Emerging adulthood is a critical developmental stage in the life course. Identifying factors associated with distinctive life course drug-use patterns will assist in developing more targeted treatment services and policies.
Financial Support: NIDA P30DA016383 & K05DA017648 (PI: Hser)

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NEIGHBORHOOD PERCEPTIONS ASSOCIATION WITH DEPRESSION.

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Aims: Several studies have linked depression to neighborhood surroundings; however, little research has examined multiple neighborhood factors in the same analysis. Among injection drug users (IDU) and non-IDU, we examined the independent relations between 4 neighborhood constructs and depression.
Methods: Individuals were recruited in Baltimore, targeting high drug use areas. This analysis used cross-sectional data from 714 individuals in 2002-2004. The sample was 41% female, 96% African American, with a mean age of 44 years. Neighborhood scales for perceived social disorder (α=0.88), perceived safety (α =0.82), perceived social control (α =0.84), and perceived future risk (α =0.82) assessed neighborhood perceptions. Depression was assessed with the Center for Epidemiologic Studies Depression scale (CES-D).
Results: In bivariate analyses, greater perceived social disorder, greater perceived future risk, and less perceived safety were all associated with higher odds of depression. In multivariable logistic regression all neighborhood scales were entered into a single regression, along with control variables, to assess the independent associations of each neighborhood construct. Greater perceived social disorder (OR: 1.37; 95% CI: 1.16, 1.62) and perceived future risk (OR: 1.54; 95% CI: 1.30, 1.82) remained associated with higher odds of depression while perceived safety (OR: 1.18; 95% CI: 0.99, 1.41) was no longer significantly associated with being depressed. Data was stratified by IDU status. Among non-IDU both social disorder (OR: 1.46; 95% CI: 1.19, 1.80) and future risk (OR: 1.30; 95% CI: 1.05, 1.62) were associated with depression. Yet among IDU, only future risk was associated with depression (OR: 1.67; 95% CI: 1.20, 2.34).
Conclusions: These analyses highlight the importance of examining specific neighborhood factors independently in association with depression. Neighborhood factors which have a differential association between IDU and non-IDU, with regard to depression may be of particular importance.
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CHARACTERISTICS OF A SAMPLE OF CAFFEINE TREATMENT SEEKERS.

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Aims: Many caffeine users endorse symptoms of substance dependence as applied to caffeine. Some daily users are unable to reduce or quit caffeine use, despite a desire to do so. The purpose of this study was to characterize a sample of caffeine treatment seekers who responded to an advertisement offering assistance to modify caffeine use.
Methods: A telephone screening questionnaire was administered to 275 caffeine users who responded to a study advertisement. Ninety-four eligible participants were invited to participate in a diagnostic screening study session. During the session, participants completed a structured clinical interview and a battery of self-report questionnaires.
Results: Mean age was 41 years. The majority of the sample was Caucasian (80%) and female (54.3%). Mean daily caffeine consumption was 547.8 mg. Eighty-one percent of the sample reported engaging in at least one past attempt to modify caffeine consumption. Ninety-seven percent reported at least one withdrawal symptom when abstaining from caffeine and 93% endorsed having used caffeine to relieve or avoid withdrawal. Significant functional impairment due to withdrawal symptoms was reported by 43% of the sample. Ninety-three percent fulfilled DSM-IV-TR criteria for substance dependence as applied to caffeine by endorsing at least three of seven diagnostic criteria with 55% endorsing at least five of seven criteria. Eighty-seven percent of the sample endorsed continuing to use caffeine despite physical or psychological problems that they believed to be caused or exacerbated by caffeine. Commonly reported problems included sleep difficulties, frequent urination, anxiety, irritation, and stomach problems.
Conclusions: The study provides further evidence that some caffeine users exhibit a pattern of symptoms consistent with substance dependence as applied to caffeine. Moreover, the study demonstrates that there is a need for treatments to assist dependent caffeine users to modify their caffeine consumption.
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A CASE-CROSSOVER APPROACH TO GATEWAY RESEARCH: FIRST CIGAR TO FIRST BLUNT SMOKING.

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Aims: In etiologic research on drug hazards, the epidemiological case-crossover design is most useful when drug use might rapidly trigger onset of a suspected hazard. Due to this design's subject-as-own-control feature, all individual-level genetic and other susceptibility traits are held constant in a focused test of the triggering hypothesis. Here, we use this design to estimate the degree to which newly-incident cigar smoking might serve as a rapid trigger for newly-incident blunt use (cannabis smoked inside a hollowed out cigar). All else being equal, if cigar smoking rapidly triggers blunt smoking, there should be excess odds of first cigar in month t-1 just before first blunt in month t, relative to odds of first cigar in month t-2 of a blunt smoker's life.
Methods: Data are from the United States National Surveys of Drug Use and Health, 2005-2007, with nationally representative samples of non-institutionalized civilian residents and standardized assessments of month-by-month onset of cigar use and blunt use among newly-incident blunt smokers (n=5143). Statistical analysis involves standard methods for estimation of risk ratios (RR) and 95% confidence intervals (CI) for matched pair data.
Results: In evidence favoring the rapid triggering hypothesis, the 1st cigar was smoked in month t-1 for 140 newly-incident blunt smokers assessed within 24 months after blunt onset in month t. In evidence against this hypothesis, 69 newly incident blunt smokers had first smoked a cigar in month t-2 (RR = 2.0; 95% CI = 1.5, 2.7; $p<0.001$). RR estimates based on other control months (e.g., t-3, t-4) did not differ appreciably. Little evidence of recall bias was found in estimates for strata formed by assessment recency (e.g., RR = 1.5; $p<0.05$ for those assessed within 6 months after blunt onset; RR = 2.2; $p<0.05$ for those assessed in months 6-12).
Conclusions: In the US, there now is a yoked cigar-blunt sequence. If replicated, this evidence on the cigar-to-blunt trigger will set a stage for research on mechanisms of excess risk.
Financial Support: NIDA support: T32DA021129 (BF); K05DA15799 (JCA)

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PERCEIVED COERCION AMONG INDIVIDUALS WHO DRIVE UNDER THE INFLUENCE OF ALCOHOL AND DRUGS: TESTING THE "ROLLING CONSENT" APPROACH APPLIED TO A NATIONWIDE TELEPHONE SURVEY.

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Aims: The validity of the consent process in research is dependable on the guarantee that there was no coercion. "Rolling consent" is obtained by steps – the respondent is informed he/she can quit the interview at every section of data collection– intending to reduce the feeling of coercion. The aim of this study was to assess the perceived coercion, using telephone interviews with rolling consent, among drivers who test positive for substance(s) and those who do not.
Methods: This was a cross-sectional study with drivers from a roadside survey who were breathalized and had their saliva tested for other drugs. Subjects (n=1,134) were later contacted by telephone for a structured interview using rolling consent methodology to obtain data on psychiatric disorders, risky behavior and perception of coercion (Perceived Coercion Scale, range 0-5).
Results: Participants who completed the interview and answered the coercion scale (n=747, 65.8%) were divided into drivers who tested positive for substances (n=55) and those who did not (n=692). Among the substance-positive drivers, only 2 (3.6%) reported score ≥ 3, compared to 86 (0.8%) among other drivers ($p=0.7$). The mean score of the Perceived Coercion Scale was 0.88, indicating a low perception of coercion in this sample.
Conclusions: Rolling consent was useful to prevent perception of coercion in this telephonic interview, showing that the drivers felt comfortable to express their disagreement during the interview. This consent form prevents the complete data disposal if the participant decides to quit the interview and the feeling of obligation, minimizing embarrassment.
Financial Support: Brazilian National Secretariat for Drug Policies (SENAD)

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THE ROLE OF TAMPER TESTING IN THE ASSESSMENT OF ABUSE POTENTIAL.

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Aims: The FDA's Draft Guidance on the Assessment of Abuse Potential recommends that Sponsors perform studies to assess methods that abusers might use to increase the amount of drug delivered, the speed of drug delivery, or allow for the use of the drug via alternate routes of administration. The current paper will present principles of tamper testing that should be considered in the evaluation of tamperability.
Conclusions: There are several principles that will be discussed in this paper. First, is consideration of the routes of administration currently employed by abusers to abuse the particular class of drug. Information on current practices can be found by reviewing data from federal surveys, the published literature, and Internet sites where drug abusers post information about their experiences with drugs. Secondly, is consideration of the tampering methods already being employed for abuse of existing drugs, including which solvents are commonly used to solubilize the drug. Thirdly, is the need for testing of a wide array of methods that might be used to crush the tablet into a powder, different solvents, testing at different temperatures and pHs, and across different timeframes. Fourthly is, interpretation of the findings with consideration given to the known behavioral and neuropharmacology of the drug to assess the biological plausibility that the method under consideration would result in a more a reinforcing and hence abusable substance or form. Behavioral economics analyses may also be considered to assess the potential real-world attractiveness and viability of the method. While it is important to determine under which conditions extraction might be possible, it is equally important to understand the cost of the process to the abuser. This paper will discuss each of these principles in detail.
Financial Support: Pinney Associates provides a wide array of consulting services for pharmaceutical companies, including tamper testing. However, all financial support related to this paper is from Pinney Associates, and no industry support has been or will be used.

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EFFICACY OF ANTIDEPRESSANTS IN ALCOHOL DEPENDENCE WITH AND WITHOUT COMORBID DEPRESSION: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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Aims: To assess the efficacy of antidepressant drugs in subjects with alcohol dependence disorders with and without a diagnosis of comorbid depression.
Methods: A systematic review and meta-analysis of randomized controlled trials (RCTs) comparing antidepressants with placebo were done following the methodology developed by the Cochrane Collaboration. A systematic search was carried out in Medline (Pubmed 1966-April 2010), Embase and Cochrane library. The abstracts were revised to select the eligible publications. The references in selected published articles, reviews and meta-analyses were checked for potential new sources. Two outcome measures: alcohol use, and improvement in depressive symptoms were analysed.
Results: Ten RCTs were included. Studies did not support the efficacy of antidepressant drugs for alcohol dependence. In the condition of alcohol dependence with comorbid depression, results of the meta-analysis showed that antidepressants improved depressive symptoms, but not alochol use.
Conclusions: Although antidepressants are commonly used in alcohol dependence, more studies are needed to confirm its usefulness. SSRI drugs do not seem to offer significant advantages compared with tricyclic drugs. The use of antidepressants in alcohol dependence with comorbid depression needs more studies in well-defined samples, adequate doses and duration of treatment to be really conclusive.
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DO GAMBLING-INDUCED DISORDERS EXIST?

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Aims: Introduction: In the context of DSM-IV revision, the possible inclusion of pathological gambling within the same classification system as substance use disorders is discussed based on clinical, demographic, biological and genetic similarities between these disorders. Among commonalities, the parallel with substance-induced disorders should be considered.
Objective: To explore the presence of gambling-induced disorders defined as disorders related to gambling practice or withdrawal from gambling.
Methods: A systematic literature review was conducted on areas relevant to pathological Gambling and its association with both psychiatric and physical symptoms.
Results: Eight studies were included. Among these studies, 6 aimed to describe gambling withdrawal-like symptoms, one study reported physical symptoms during gambling and one study assessed gambling-induced depressive symptoms. Depressive symptoms ranged from 20 to 39 of subjects % after gambling cessation, with higher prevalence among pathological gamblers (20 to 70 %). Significant somatic disturbances were reported by gamblers (sleep problems, headaches, gastro-intestinal symptoms) when attempting to quit gambling.
Conclusions: Data supported the presence of both depressive and physical symptoms attributed to gambling or withdrawal from gambling with higher rates being associated with gambling severity. The phenomena of substance-induced disorders may have direct parallel in pathological gambling. The issue of psychiatric symptoms as direct negative consequences of gambling should be further assessed.
Financial Support: PRA-CNRS (2009-2011) to M. Fatséas
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UTILIZATION OF AN AUTOMATED THERAPEUTIC TELEPHONE SYSTEM IN PRIMARY CARE BUPRENORPHINE.

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Aims: The Recovery Line is an automated telephone-based voice response system for opioid dependent patients receiving buprenorphine. The system is based on cognitive behavioral therapy and includes modules that provide immediate coping activities as well as instruction in identifying patterns and avoiding use. Patients receive 24-hour access and have free choice of system navigation and were asked to rate helpfulness of each activity upon completion. We evaluated call patterns, module access, and within-call feedback to determine which components are most useful to patients in their natural environment.
Methods: Analyses were based on 1740 minutes of total call time from 10 pilot patients new to buprenorphine treatment. Patients had access to the system for 4 weeks and were instructed to call daily.
Results: Patients had a mean of 191.2 min of therapeutic contact time and made a mean of 15.2 total calls. Mean call length was 13.7 min (SD = 10). Patients utilized the 24-hour system availability: over half (52%) of calls were made outside of normal business hours (9:00-5:00pm). Of 500 instances of modules access, the most frequented sections were coping with craving (31%), relaxation and stress management (22%) and encouragement/motivation (22%). Sections that were attended less frequently included functional analysis of substance use behavior (3%) and mindfulness (8%). Patients had high within-call activity ratings of helpfulness, with 70% of activities rated high (4) or very high (5). Highest patient ratings were for relaxation and stress management modules (M=4.4).
Conclusions: Within high utilization of a therapeutic interactive voice response system, patients frequently attended modules that focused on immediate craving, stress management, and encouragement/motivation. Within-call ratings of activities were also high and consistent with module access. These findings suggest the system provides an immediate coping tool for patients in their environment. Future evaluation will examine the relationship between patient system use and drug use behavior.
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USING FMRI TO EVALUATE ADOLESCENTS' RESPONSE TO A PSYCHOSOCIAL CANNABIS TREATMENT.

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Aims: Cannabis is the most abused substance in juvenile justice populations, with almost half (45%) of justice-involved youth meeting cannabis use disorder criteria. At present, psychosocial cannabis interventions are only modestly effective. Adolescent studies suggest that one ingredient may influence treatment response: client language. This study evaluated the relationship between in-session client language (change talk; CT and sustain talk; ST) and brain activation during an fMRI-based cue-exposure. It was posited that CT would be associated with less activation in reward areas than ST.
Methods: Adolescent cannabis abusers (N=25; M age=16; 76% male; 68% Hispanic) received one audio-recorded session of MI followed by an fMRI scan. All participants were re-presented with their in-session CT and ST statements by sight and sound during the tactile fMRI-based cannabis cue-exposure.
Results: This sample included cannabis abusers, as evidenced by their cannabis use history (M age of first use=11.70 years old) and past month use (M=21.19 cannabis use days). Both types of client language (CT and ST) resulted in significant activation in the thalamus, parietal, and cerebellar areas during the control condition (max Z =5.48; 4.64, respectively). Moreover, during exposure to the cannabis cue, significantly greater activation emerged during the CT (max Z=5.75; VTA, insula, putamen, cingulate gyrus/SMA, superior frontal gyrus) versus the ST condition (max Z= 5.08).
Conclusions: These results suggest that within this sample of justice-involved adolescent cannabis abusers, salient reward areas, as well as key executive control areas, are significantly activated when participants processed CT in response to the cannabis cue. The activation differs from our prior studies with older and alcohol-using samples, and underscores the importance of evaluating client language in younger samples, and across substances of abuse.
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GENDER DIFFERENCES IN EARLY AGE OF ONSET OF ALCOHOL AND TOBACCO USE AS A RISK FACTOR.

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Aims: The aim of this study was to assess the different predictive value for boys and girls of early onset of use of alcohol and tobacco for illegal drugs use and psychosocial consequences.
Methods: Information was obtained by a self-reported questionnaire applied to 1190 students aged 16-18 years (562 girls) from the Principality of Asturias (Spain). Logistic Regression analyses (CI: 95%) were undertaken to determine the predictive value of early age of onset of tobacco and alcohol use on other drugs use (cannabis, cocaine, ecstasy, amphetamines, hallucinogens and getting drunk), as well as the last year prevalence of several psychosocial problems (family conflict, being robbed, running away from home, being expelled from school, being involved in accidents and fights, receiving urgent medical assistance and being detained).
Results: Results support early age of onset of tobacco use as significant predictor for both genders for ever using cannabis (or: 1.7 for boys, 2.3 for girls), cocaine (2.6 vs 10.9) and ecstasy (4.9 vs 8.7) and being involved in fights (2.2 vs 4.2). For girls, it also predicted amphetamine (or: 8.7) and hallucinogens use (or: 18.6). Early alcohol use was a predictor in boys and girls of all drugs use, and for boys it also predicted being expelled from school (or: 2.8) and involved in fights (or: 2.2). For girls, early alcohol use also predicted family conflict (or: 1.8) and urgent medical assistance (or: 2.0).
Conclusions: As early alcohol and tobacco use showed a significant and differential effect on predicting other drugs use and psychosocial problems, it is important to consider sex differences when assessing risk factors for adolescent drug use. Early alcohol use seems to be a stronger predictor of any drug use for boys, whereas early tobacco use is a stronger predictor of all assessed variables for girls. Future studies shall use longitudinal designs to verify these results and assess any underpinning mediator variables.
Financial Support: Ministry of Science and Innovation of Spain. Project No: MICINN-08-PSI2008-00309

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COMBINING REMEDIAL AND MOTIVATIONAL STRATEGIES TO IMPROVE CONSENT RECALL AMONG RESEARCH PARTICIPANTS.

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Aims: This study examines the effects of combining both incentivized consent and corrected feedback on participants' recall of consent information. Despite the significant effects of corrected feedback observed in our previous research (Festinger et al., 2010), participants recalled only 65% of consent information, suggesting that remedial approaches alone may be insufficient. In addition to cognitive deficits which may be addressed by remedial strategies, it is possible that some participants may be unmotivated to recall consent information. In a preliminary study (Festinger et al., 2009) we found that an incentivized procedure where participants received $5.00 for each question they answered correctly on a consent quiz one week later, participants recalled significantly more information than a non-incentivized group with a large effect size (> 1 SD).
Methods: We randomly assigned 80 subjects into two different consent conditions: (1) consent process as usual, and (2) consent process with incentives and corrected feedback. Both groups received the standard informed consent procedure at baseline and at months 1, 2, 3, 4, and 6. Participants in the experimental group were informed prior to consent that they would earn a 5$ money order for each item that they answered correctly on the 15-item post-intake consent quiz (possible total of $75.00). They also received corrected feedback on all incorrect responses.
Results: Results supported our original hypothesis with the experimental participants displaying an average increase in recall from 68.1% to 79.6% after 4 administrations, compared to control participants who displayed a decrease in recall from 71.3% to 64.2%.
Conclusions: Results indicate tha itility of a novel strategy for improving consent recall in research studies. Results also provide an important "proof-of-concept" regarding whether motivational procedures are required to obtain an acceptable level of mastery of consent information.
Financial Support: NIDA Grants R01 DA-016730 and R01-DA-013096.

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RELATIONSHIP BETWEEN WEIGHT STATUS AND DELAY DISCOUNTING IN A SAMPLE OF ADOLESCENT CIGARETTE SMOKERS.

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Aims: Obesity and cigarette smoking are often cited separately as the top two preventable causes of death in the US; however, little research has explored factors associated with being both obese and a smoker. Delay discounting is a behavioral characteristic that may underlie both of these conditions/behaviors. Delay discounting describes the extent to which an individual discounts the value of an outcome because of a delay to its occurrence. Higher rates of discounting are often considered an index of impulsivity and have been linked with obesity and cigarette smoking. No research to date has explored delay discounting in a sample obese smokers.
Methods: For the current study, adolescent smokers classified as obese (BMI greater than 95th percentile) or healthy-weight (BMI between the 5th and 85th percentiles) were compared on a laboratory assessment of delay discounting.
Results: Obese smokers discounted significantly more by delay than healthy-weight smokers [$F(1, 34) = 7.36$, $p < .01$]. This difference remained statistically significant even after controlling for demographic variables that differed across groups.
Conclusions: These findings suggest the relationships between delay discounting and obesity and cigarette smoking may be additive, such that extreme discounting might proportionally increase risk of becoming an obese smoker.
Financial Support: This research was supported by NIH grant NIDA R01 DA023087-01A2

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REPEATED INTERMITTENT TREATMENT WITH THE SELECTIVE 5-HT$_{2C}$R AGONIST WAY 163909 PRODUCES BEHAVIORAL TOLERANCE TO ITS ACUTE HYPOMOTIVE EFFECTS.

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Aims: Dysregulation in limbic-corticostriatal serotonin (5-HT) 5-HT$_{2C}$ receptor (5-HT$_{2C}$R) function is implicated in a variety of neuropsychiatric conditions, including substance use disorders. Selective 5-HT$_{2C}$R agonists reduce psychostimulant consumption and cue-evoked reinstatement in rodent self-administration models, underscoring the potential clinical utility of 5-HT$_{2C}$R agonists as treatment adjuvants for psychostimulant dependency. However, altered 5-HT$_{2C}$R sensitivity in response to repeated agonist administration may prove counterproductive under pharmacotherapeutic conditions. We sought to explore the molecular and behavioral response to repeated, intermittent treatment with the selective 5-HT$_{2C}$R agonist Way 163909.
Methods: Male Sprague-Dawley rats were treated once daily for 7 days with saline (1 mL/kg, i.p.) or Way 163909 (10 mg/kg, i.p.). Weights were recorded daily. On day 8, rats from both treatment groups were randomly assigned to receive either a challenge treatment of saline or Way 163909 (10 mg/kg, i.p.), and locomotor activity was measured for 90 minutes. Brain tissue was immediately collected and frozen for future biochemical analysis of 5-HT$_{2C}$R expression.
Results: Acute treatment with Way 163909 significantly reduced total horizontal activity compared to saline controls ($p<0.05$). Repeated Way 163909 administration blunted the magnitude of the hypomotility induced upon acute Way 163909 challenge ($p<0.05$).
Conclusions: These results indicate that repeated Way 163909 treatment induces a behavioral tolerance to the acute hypomotive effects of a 5-HT$_{2C}$R agonist, suggesting reduced 5-HT$_{2C}$R function, potentially as a result of underlying receptor desensitization mechanisms.
Financial Support: DA06511, DA020087, DA024157 and DA07287

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PHYSICAL DEPENDENCE FOLLOWING ACUTE BENZODIAZEPINE ADMINISTRATION: ROLE OF α1GABA$_A$ RECEPTORS.

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Aims: The present study established a model of benzodiazepine physical dependence using an assay of schedule-controlled responding, and also investigated the role of GABA$_A$ receptor subtypes in mediating dependence-like effects.
Methods: Squirrel monkeys were trained on a fixed-ratio schedule of food reinforcement. Initially, the response rate-decreasing effects of chlordiazepoxide (nonselective GABA$_A$ receptor agonist), zolpidem (α1 subunit-containing GABA$_A$ (α1GABA$_A$) receptor agonist), and HZ-166 (α2 and α3 subunit-containing GABA$_A$ (α2,3GABA$_A$) receptor agonist) were assessed. Next, acute dependence following chlordiazepoxide, zolpidem, and HZ-166 was assessed with flumazenil (nonselective GABA$_A$ receptor antagonist). Finally, acute dependence following zolpidem administration was assessed with βCCt and 3-PBC (α1GABA$_A$ receptor antagonists).
Results: Chlordiazepoxide and zolpidem produced dose- and time-dependent decreases in response rates, whereas HZ-166 was ineffective. After the drug effects waned, flumazenil produced dose-dependent decreases in response rates following administration of chlordiazepoxide and zolpidem, but not HZ-166. Further, both βCCt and 3-PBC produced dose-dependent decreases in response rates when administered after zolpidem.
Conclusions: These data demonstrate that flumazenil can precipitate disruption of schedule-controlled behavior after acute treatment of a benzodiazepine. At least two findings suggested that this effect involved α1GABAA receptors. First, flumazenil was effective at decreasing response rates following an α1GABA$_A$ receptor agonist but not an α2,3GABA$_A$ receptor agonist. Second, two α1GABA$_A$ receptor antagonists were shown to precipitate disruption of schedule-controlled behavior after acute treatment with an α1 GABAA receptor agonist. Together, these findings raise the possibility that a single injection of a benzodiazepine is sufficient to produce physical dependence, and suggest further that this effect is likely mediated by α1GABA$_A$ receptors.
Financial Support: Support: DA011792, RR000168, MH046851.

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SCREENING, BRIEF INTERVENTION, AND REFERRAL TO TREATMENT FOR DRUG- AND ALCOHOL-RELATED HEALTH PROBLEMS IN EMERGENCY DEPARTMENTS: REVIEW OF OUTCOMES, IMPLEMENTATIONS, AND FEASIBILITY.

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Aims: Review of relevant research on SBIRT in ED settings regarding intervention effectiveness, potential cost-savings, and implementation.
Methods: Publications referring to SBIRT in ED settings in either primary research or review were selected and were parsed into 3 categories: outcomes, cost feasibility, and implementation. Some articles were included in more than one category. Outcome literature excluded review publications and focused on primary analyses of SBIRT in ED settings targeting drug and alcohol use.
Results: Outcomes: 17 articles were found and were separated into interventions for alcohol vs. drug with some studies appearing in both groups. Of the 13 alcohol studies, 12 reported reductions in alcohol use. Of the 6 drug studies, 4 reported reductions in drug use. Those studies not reporting reductions in alcohol or drug use identified treatment attendance as the outcome variable, with all reporting higher levels of treatment attendance. Cost Feasibility: Findings outlined several cost-saving advantages, including meeting unmet needs among ED patients with SUDs and reducing recurrent substance-related ED visits. Implementation: 14 publications discussed aspects of SBIRT implementation in ED settings. Considerable support exists for screening and intervention methods. Research indicates that screening and intervention can be quickly and effectively conducted by doctors and mid-level providers. Although SBIRT has been successfully integrated into many busy EDs, it is a challenge that requires ongoing commitment, planning, and support from ED staff.
Conclusions: Though barriers exist in SBIRT implementation, EDs using an SBIRT approach have shown overall cost savings in addition to improved ability to diagnose and treat substance-use related problems. More research is needed to explore the effect of SBIRT in EDs as an intervention for drug related problems as well as the long-term sustained implementation.
Financial Support: NIDA CTN

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HIV RISK BEHAVIORS AMONG GAY AND BISEXUAL MEN OVER A WEEKEND VACATION.

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Aims: There is a strong relationship between drug use and unprotected anal intercourse (UAI), behaviors that are heightened during weekend vacations. In this study, we describe party-goers' intentions to use drugs and expectations of having UAI over a "party vacation", their actual behaviors over the weekend, and the relationship between these constructs. We hypothesize that most weekend drug use is intended; when accounting for expectations to have UAI, independent effects between drug use and UAI are attenuated.
Methods: 489 gay and bisexual men arriving at weekend "party vacations" were randomly recruited to participate in an anonymous survey. Of these, 47% completed the follow-up assessment. Descriptive statistics were compiled; multivariate regression was used to assess correlates of UAI.
Results: At baseline, 45% of respondents intended to use ecstasy over the weekend, and intentions to use GHB, marijuana, cocaine or crack, and unprescribed erectile dysfunction drugs (EDDs) were each over 20%. Close to 50% reported having UAI in the past year and almost 20% also expected to have anal intercourse (AI) over the weekend and not being "very likely" to use a condom every time they did. At follow-up, prevalence of weekend drug use followed the same patterns as drug use intentions; 33% had AI over the weekend and approximately one-third did not use a condom at least once. Having had UAI in the past year predicted UAI over the weekend (Odds Ratio=4.65, $p<0.05$) though in models accounting for past year UAI there was no association between drug use and UAI.
Conclusions: Having had UAI in the past year is a stronger predictor of UAI over the weekend than either intentions to have UAI or drug use. However, having had UAI in the past also predicts expecting to have UAI over the weekend, which is correlated with intending to use drugs. Collectively these findings suggest a more complex relationship between drug use and HIV risk than simply impaired decision-making as a consequence of drug use.
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TREATMENT OUTCOMES WITH RELAPSE PREVENTION MEDICATIONS FOR OPIOID DEPENDENCE IN YOUTH.

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Aims: This study describes the association between use of relapse prevention medications and treatment outcomes over 26 weeks in youth with opioid dependence in a community treatment program.
Methods: Data was abstracted retrospectively from clinical charts of 133 patients admitted between 4/07 and 1/10 to the adolescent/young adult outpatient opioid track at Mountain Manor Treatment Center in Baltimore MD.
Results: Patients characteristics included: 54% male, 94% Caucasian, mean age 18.2 years (range 14-21), mean duration of opioid use 2.8 years, 61% injection use. Although the mean retention until initial dropout (defined as 2 weeks without any treatment contact) was 9.6 weeks, 49.3% of patients returned to treatment after dropout, with 1.9 mean episodes of treatment and mean cumulative retention of 13.5 weeks. 61% took relapse prevention medications (39% buprenorphine, 19% extended release naltrexone, and 3% oral naltrexone). Mean cumulative retention was 15.8 weeks for those on any relapse prevention medication vs. 10.3 weeks for those on no medication ($p= 0.0001$), 16.3 weeks for those on extended release naltrexone ($p = 0.0008$), 15.9 weeks for those on buprenorphine ($p = 0.0002$). Mean cumulative time without opioid use (combining self-report and urine testing) was 11.5 weeks for those on any relapse prevention medication vs. 7.0 weeks for those on no medication ($p=.0003$), 13.7 weeks for those on extended release naltrexone ($p < 0.0001$), 10.6 weeks for those on buprenorphine ($p = .009$).
Conclusions: Medication treatment for adolescent/young adult opioid dependence is feasible and effective in a community treatment setting. Use of medications for relapse prevention seems to be associated with increased retention and opioid-free weeks over the 1st 26 weeks of treatment in this population in a small, non-randomized sample.
Financial Support: Supported by: Mountain Manor Treatment Center.

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APATHY AS A MODERATOR OF THE ASSOCIATION BETWEEN SOCIAL DISORGANIZATION AND SEX WITH MEN INVOLVED IN DRUG DEALING.

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Aims: Research indicates the attributes and behaviors of male sexual partners available to African American women is likely related to their increased risk for contracting STDs, including HIV. Because of their social and economic position, which often affords them access to more sexual partners and persons at high risk for HIV infection, drug dealers may be considered high risk sexual partners. The purpose of this study was to identify factors associated with sex with male drug dealers. We considered the influence of neighborhood social disorganization and psychological factors.
Methods: Employing a cross sectional design 120 Black females were administered a semi-structured interview and tested for STDs.
Results: Approximately 32% thought drug dealers in their neighborhood have the most money,57% indicated drug dealers have the most women,60% had sex with a male involved in drug dealing, 46% used marijuana and 7% tested positive for an STD. Results from binary logistic regression analyses indicated an interactive effect of social disorganization and apathy on high risk sexual partnerships. Among females who were more apathetic those who perceived their neighborhoods as more socially disorganized had an increased odds of having sex with a drug dealer (AOR = 2.9; 95%CI = 0.9 - 9.5) and were 3.6 times more likely to have sex with a male incarcerated for selling drugs (95%CI = 1.11 – 11.93).
Conclusions: The influence of the drug epidemic on HIV risk may extend beyond core members of illicit drug networks. A high percentage females reported sex with drug dealing males who were thought to have many female sexual partners. Living in more socially disorganized neighborhoods increased the likelihood of having sex with a drug dealer for females who experienced apathy. Females living in socially disorganized neighborhoods who have poor psychological functioning may be at increased risk for engaging in high risk sexual partnerships. More research is needed to examine sexual behaviors of male drug dealers and to identify modifiable psychological protective factors for at-risk females.
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COCAINE-DEPENDENT PATIENTS SEEKING TREATMENT: RETENTION AND ABSTINENCE RATES.

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Aims: To describe retention in treatment and cocaine abstinence rates at 6 months in patients entering to treatment for cocaine dependence.
Methods: Prospective study. All cocaine dependent patients (DSM-IV) entering to an out-patient program were consecutively recruited and followed for 6 months. Socio-demographical, medical and psychiatric comorbidity variables were assessed. Patients' outcome was assessed in terms of retention and cocaine use detected in random urinalysis.
Results: A total of 65 cocaine dependent patients were included (72.3% males, mean age: 36+9 years). Cocaine was mainly snorted (73%). Age of onset of cocaine use: 21+7 years. The majority of the patients presented other substance related disorders (nicotine dependence: 88%; alcohol dependence: 22%. Psychiatric comorbidity was detected in 46% patients. Retention rates were 42% and abstinence rates (among those retained) were 70%. There were no differences in the characteristics between retained and non-retained patients.
Conclusions: Retention rates in a sample of patients asking for cocaine dependence treatment in a specialized center are less than 50%. Strategies focused in patients' retention are needed.
Financial Support: Fondo de Investigación Sanitaria, Instituto Carlos III (ISCIII: GO3/184, 06/0001/1009).

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THE RELATIONSHIP BETWEEN THERAPIST AND PATIENT GENDER/RACE MATCHING AND SUBSTANCE USE OUTCOMES ACROSS TWO MET TRIALS.

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Aims: Although some research supports patient/therapist similarity in developing a therapeutic alliance more successfully, findings are mixed. The aim of this study was to examine the moderating effects of gender/race matching between therapists and patients on alliance and substance use outcomes.
Methods: Identical measures were obtained in two CTN trials of MET (CTN 0004 and CTN 0021). Participants were patients (valid N=344) and therapists (valid N=24) participating in these trials who had complete data from the HAQ (measuring therapeutic alliance), ASI-lite data at baseline and week 4 (Post-treatment), and indicated perceptions of their provider's race and gender on a post-treatment questionnaire. We hypothesized that patients' perception of their therapists' race and gender would (1) affect post-treatment substance use, and (2) moderate the relationship between therapeutic alliance, defined by patient and therapist scores on the HAQ-II, and substance use.
Results: The relationship among the variables was examined using ANCOVAs. Racially matched patients reported significantly fewer days of drug use ($p = 0.02$, $d = -0.26$). However, racial match was unrelated to patient perceived alliance ($p = 0.52$). When HAQ-II therapists' scores were included in the model, racially matched patients again reported significantly fewer days of drug use ($p = 0.02$, $d = -0.26$). Race matching significantly moderated the relationship between the alliance perceived by therapists and substance use ($p = 0.04$, $d = 0.22$). Gender matched patients reported significantly more days of drug use ($p = 0.03$, $d = 0.23$) even after HAQ-II therapists scores were included in the model ($p = 0.045$, $d = 0.22$). Gender similarity did not significantly affect the level of alliance indicated by patients ($p = 0.09$) or therapists ($p = 0.58$).
Conclusions: Findings from this study support racial but not gender matching.
Financial Support: NIDA CTN

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PERINATAL SMOKING AND MOOD AND ANXIETY DISORDERS.

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Aims: Understanding the factors that influence smoking in pregnancy and the postpartum is important for the development of effective interventions. The purpose of this prospective study was to evaluate the course of smoking across the perinatal period and examine the possible moderating role of mood and anxiety disorders. We hypothesized that women with mood or anxiety disorders would be more likely to smoke and less likely to reduce their level of smoking compared to those without a comorbid disorder.
Methods: We evaluated 181 pregnant women who endorsed use of hazardous substances, including smoking. The disorder group was defined as having one or more mood or anxiety disorders in pregnancy or 3 months postpartum, all others comprised the no disorder group. We used a repeated-measures logistic regression to model use/nonuse by disorder group, and repeated-measures ANOVA to model number of cigarettes smoked by disorder group. The models included a term for time, group and the group by time interaction while adjusted for age, race/ethnicity, education and parity.
Results: Women in the disorder group were over twice as likely to smoke as those in the no disorder group (OR=2.27; 95% CI: 1.15-4.47; p=0.02) at the beginning of pregnancy. Smoking decreased in both groups as pregnancy progressed, and by month 5 smoking levels were similar ($0.80 \leq OR \leq 1.15$; $p \geq 0.54$) between groups. Cigarette use in month 3 postpartum among women without a disorder rose marginally above baseline levels, while the use among women with a disorder were still marginally below baseline levels. Similar trends were found with the adjusted mean differences for average daily cigarette use over time by disorder. Overall, from month 1 of pregnancy to month 3 postpartum, the disorder group decreased consumption by over 3 cigarettes more than did the no disorder group (MD=-3.13; 95% CI -5.33- -0.93; p=0.01).
Conclusions: Smoking was common among our cohort of pregnant women. Women in the disorder group had a higher baseline proportion of cigarette use. Contrary to our hypothesis, both groups decreased smoking during pregnancy with a proportional increase postpartum.
Financial Support: R01 DA019135-03 PI:Yonkers

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DISCRIMINATIVE STIMULUS EFFECTS OF PROPOFOL.

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Aims: Propofol is used as a surgical anesthetic and sedative, but is currently not a controlled substance. Little is known about it's mechanisms of actions, behavioral effects besides anesthesia, and abuse liability. The purpose of the present study was to determine whether propofol produces a discriminable stimulus and what receptor mechanisms mediate the discriminative stimulus effects.
Methods: Twenty-four male Sprague-Dawley rats were trained to discriminate propofol from vehicle (2% methylcellulose) using a two-lever choice methodology. Ten rats were trained at 10 mg/kg propofol, and fourteen were initially trained at 5 mg/kg. Single doses of carisoprodol (100 mg/kg), chlordiazepoxide (10 mg/kg) and dizocilpine (0.1 mg/kg) were tested for substitution for the discriminative stimulus effects of propofol (10 mg/kg). Pentylenetetrazol (10 mg/kg) was tested for antagonism of the discriminative stimulus effects of 10 mg/kg propofol.
Results: Drug-lever responding remained at chance levels for the 5 mg/kg group for 44 training sessions, so the training dose was increased to 10 mg/kg. Propofol was tested in doses from 1 to 10 mg/kg and a dose effect curve was established (ED50= 2.86 mg/kg). Carisoprodol produced 59% propofol-appropriate responding, chlordiazepoxide 65%, and dizocilpine 34%. Pentylenetetrazol decreased propofol-appropriate responding to 41%. There was substantial lethality during the course of the study. Post-mortem examination revealed cardiovascular abnormalities similar to those observed in propofol-infusion syndrome in humans.
Conclusions: Propofol can be trained as a discriminative stimulus. It's effects are most similar to GABA-A receptor compounds; however, other receptors are likely also involved. Other effects on the cardiovascular-renal system lead to substantial lethality. Exposure to low dose propofol before higher doses may be protective. Having discriminative stimulus effects similar to known drugs of abuse and a high mortality rate suggest propofol has substantial risk for misuse and abuse.
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IDENTIFYING TRAITS THAT TRACK WITH AN INCREASED RISK FOR ADDICTION VULNERABILITY.

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Aims: Patterns of individual differences in novelty-responsivity and impulsivity can be seen with respect to drugs of abuse such that individual sensitivity seems to determine the likelihood that drug use will escalate into dependence.
Methods: Male rats were screened in two assays 1) low-light open field and 2) one-choice serial reaction time task (1-CSRTT) to assess novelty response and impulsivity, respectively. The upper and lower 25% of rats were identified based on total ambulation as high responders (HR) or low responders (LR) to novelty. For the 1-CSRT task, rats were maintained at ~90% free-feeding weight and trained on a 5-sec intertrial interval (ITI) and then subjected to an 8-sec ITI challenge session to more readily detect impulsive action. The upper and lower 25% of rats were identified based on premature responses on ITI8 as high impulsive (HI) or low impulsive (LI). Rats were then trained to self-administer (SA) cocaine at a low dose (0.25 mg/kg/inf; 60 min/day; FR1; 14 days) and re-trained at a higher dose (0.75 mg/kg/inf; 180 min/day; FR1-5; 5 days). Following acquisition, rat underwent daily extinction sessions and, upon reaching extinction criteria (<15 active lever presses x 3 days), were tested for cue reinstatement.
Results: HR rats were more likely to be HI (HR/HI) and LR rats were more likely to be LI (LR/LI). HR/HI rats acquired cocaine SA (10.2 ± 0.2 days) more rapidly than LR/LI rats (13.2 ± 0.5 days; $p<0.05$). Cocaine intake was higher in HR/HI rats (2.12 ± 0.5 mg/kg/day) vs LR/LI rats (0.97 ± 0.2 mg/kg/day; $p<0.05$). No phenotypic difference between HR/HI and LR/LI rats was observed for cue reinstatement.
Conclusions: The high novelty-seeking and high impulsivity phenotypes are interrelated and may have similar neurochemical underpinnings which may potentially contribute to the vulnerability to develop cocaine dependence.
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INTERACTIONS BETWEEN THE SEROTONIN RECEPTOR AGONIST 1-(2,5-DIMETHOXY-4-METHYLPHENYL)-2-AMINOPROPANE (DOM) AND HEROIN: I.V. SELF ADMINISTRATION.

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Aims: Aims: Serotonin (5-HT) systems are involved in pain modulation and drugs acting on 5-HT receptor subtypes (e.g. 5-HT2A) enhance the antinociceptive effects of opioids. It is unclear whether other (e.g., abuse related) effects of opioids are also enhanced by drugs acting on 5-HT systems. This study examined the effects of non-contingent and contingent administration of the 5-HT2A receptor agonist 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) on i.v. heroin self-administration in rhesus monkeys.
Methods: Methods: Four rhesus monkeys responded under a fixed ratio 30 (180-second timeout) schedule of i.v. drug delivery in daily 90-minute sessions to receive different doses of heroin alone (0.0001-0.1 mg/kg/injection), heroin after a non-contingent injection of DOM (0.1-0.32 mg/kg), DOM alone (0.0032-0.032 mg/kg/injection), or heroin and DOM in combination.
Results: Results: Self administration of heroin alone yielded an inverted U-shaped dose response curve with monkeys receiving a maximum of 20-25 heroin injections per session; on average monkeys received fewer than 8 injections of saline per session. Non-contingent administration of DOM (5 minutes prior to sessions) increased responding for saline and for small doses of heroin in three monkeys and only decreased responding in the fourth monkey. Contingent injections of DOM failed to maintain responding above what was observed with contingent injections of saline. With increasing doses of DOM in the DOM/heroin mixture, self administration responding was only suppressed with no indication of a leftward shift in the heroin dose-response curve.
Conclusions: Conclusions: These data suggest that, although DOM alone does not have significant positive reinforcing effects under these conditions, DOM might enhance these effects of heroin. Thus, combined use of opioids and 5-HT receptor agonists for treating pain might be limited by the increased abuse potential of such combinations.
Financial Support: Support: USPHS Grants DA05018 and DA07918

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CAN AN ACUTE DOSE OF BACLOFEN REDUCE THE RISK OF RELAPSE IN CUE-VULNERABLE SMOKERS?

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Aims: Preclinical studies confirm that the GABA B agonist, baclofen blocks dopamine release in the reward-responsive ventral striatum (VS) and medial prefrontal cortex, and consequently, blocks drug motivated behavior. In humans baclofen shows potential as a medication to treat alcohol, cigarette and other addictions, however its effects on the human brain were unknown. Thus, in previous work we utilized a laboratory model that included a 3-week medication versus placebo regimen to examine its actions on brain circuitry. Using perfusion fMRI, a quantitative method that allows the examination of longitudinal medication-induced changes, resting baseline scans were acquired before and after the medication regimen. Chronic baclofen dampened baseline activity bilaterally in the VS, insula and medial orbitofrontal cortex (mOFC). We hypothesized that one dose of baclofen might have similar effects in the brain at rest.
Methods: To test whether the baclofen-induced effects were due to long-term or acute alterations in brain function, we administered either one 20 mg dose of baclofen or no medication (control condition) to N=11 smokers in a within subjects design and acquired resting baseline scans under both conditions.
Results: Similar to chronic baclofen, acute baclofen blunted VS, mOFC and amygdala activity in the brain at rest, without differences in sedation across conditions.
Conclusions: These results have important clinical implications as they demonstrate that acute baclofen is effective at blunting limbic circuitry. Smokers can often control their craving as evinced by the fact that they can remain abstinent for months or even years after quitting. Given that relapse may occur long after withdrawal symptoms abate and chronic medication may not be a practical solution in these 'cue vulnerable' smokers, acute baclofen may suffice to immediately block drug-motivated behavior during 'at risk' situations.
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SELF-ADMINISTRATION OF COCAINE AND REMIFENTANIL BY MONKEYS UNDER CONCURRENT ACCESS CONDITIONS.

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Aims: Among drug abusers, the cocaine-opioid combination is often preferred to either drug alone. Laboratory research has focused largely on the reinforcing effects of the combination relative to the single drugs. However, little research has been done on drug mixing under conditions allowing concurrent access. The present study investigated self-administration of cocaine and the short-acting mu opioid agonist, remifentanil, when the drugs were concurrently available. It was hypothesized that monkeys would adjust their responding as doses were changed to maintain consistent intake of the two drugs.
Methods: Using a two-lever design, four male rhesus monkeys were allowed to self-administer cocaine (100 or 200 μg/kg/inj) on one lever and remifentanil (0.05-0.4 μg/kg/inj) on the other, each under a FR10 schedule of reinforcement. Daily sessions lasted 2-h, and post-injection time-outs were set at 11-sec to cover the 10-sec duration of drug injections.
Results: When saline was an alternative, responding on the saline-associated lever was low relative to the drug alternative. When cocaine and remifentanil were concurrently available, monkeys generally self-administered both drugs above saline levels. However, whole-session drug intake for cocaine and remifentanil was dose-dependent in that larger doses of a drug generally resulted in greater intake of that drug. Furthermore, as the dose of one drug was increased, the intake of the other drug generally decreased.
Conclusions: These data indicate that monkeys will self-administer cocaine and an opioid concurrently. However, given that drug intake varied by dose for both drugs, there was no indication that monkeys maintained a set cocaine:opioid intake ratio when both drugs were available.
Financial Support: This research was supported by R01-DA-019471 from the National Institute on Drug Abuse.

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DISCRIMINATIVE PROPERTIES AND CYTOTOXICITIES OF CANNABINOID RECEPTOR AGONIST CP 55,490.

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Aims: The aim of the present study was to investigate the behavioral and cytotoxicological properties of cannabinoid receptor agonist CP 55,490 (CP55) in mice.
Methods: C57BL/6J mice were trained to discriminate CP55 (0.1 mg/kg i.p.) from vehicle while responding under a fixed ratio 10 schedule of food presentation. The cytotoxicological effects of CP55 were characterized in NG108-15 cells. At 24h, cytotoxicity was measured using the Cytotox-Glo cytotoxicity assay kit purchased from Promega.
Results: C57BL/6J mice were trained to discriminate CP55 from vehicle. During the tests, CP55 dose-dependently increased drug-appropriate responding with the training dose (0.1 mg/kg) producing a mean+S.E.M. of 97+1% of CP55-appropriate responses. Administration of delta9-tetrahydrocannabinol (delta9-THC) also dose-dependently increased CP55-appropriate responding to a mean of 100% at doses of 3 mg/kg. Pretreatment with cannabinoid CB1 antagonist AM251 significantly antagonized the discriminative effects of CP55 and delta9-THC. The discriminative stimulus effects of CP55 and delta9-THC are mediated by CB1 receptors. Administration of CP55 in NG108-15 cells caused cell death in a dose-dependent manner. The neurotoxic effects of CP55 were antagonized by pretreatment with CB1 antagonist AM251.
Conclusions: Our findings demonstrated that cannabinoid CB1 receptors might be involved in the expression of CP55-induced discriminative stimulus effects. The discriminative stimulus effects of CP55 were similar to the effects of delta9-THC cue. The discriminative stimulus effects of CP55 in mice could be used to evaluate mechanisms of cannabinoid activity. Furthermore, our data on NG108-15 cells indicate that CP55 neurotoxicity appears to be mediated by CB1 receptors. The NG108-15 cell line is a good model system for studying cytotoxicological properties of the cannabinoid receptor agonist.
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THE GROWTH OF NEIGHBORHOOD DISORDER AND MARIJUANA USE AMONG URBAN ADOLESCENTS TRANSITIONING INTO YOUNG ADULTHOOD: MAKING A CASE FOR POLICY AND ENVIRONMENTAL INTERVENTIONS.

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Aims: This study examines the growth of neighborhood disorder and subsequent marijuana uses among urban adolescents transitioning into adulthood.
Methods: Data are derived from a longitudinal sample of 434 predominately African American 12th graders followed 2 years post-high school. The data are rich in repeated measures documenting substance use and misuse and neighborhood characteristics. Growth mixture modeling (GMM) was used to examine how neighborhood disorder trajectories, measured through the presence of abandoned buildings on the blocks where participants reside, influences subsequent drug use beginning in late adolescence and into young adulthood.
Results: A four-class solution characterizing neighborhood growth was selected as the final model and included rapidly-improving, slightly-improving, always-good, and deteriorating neighborhoods. Young adults living in neighborhoods that had been deteriorating over time were 30% more likely to use marijuana two-years post high school than adolescents living in always-good neighborhoods (OR=1.30, p=0.034). There was no relationship between living in a neighborhood that was improving and marijuana use.
Conclusions: This study identified a salient and malleable neighborhood characteristic, abandoned housing, which predicted elevated risk for young adult marijuana use. This research supports environmental strategies that target abandoned buildings as a means to improve health and health behaviors for community residents, particularly young adult substance use.
Financial Support: National Institute on Alcoholism and Alcohol Abuse (NIAAA) R01AA015196 and the National Institute on Drug Abuse (NIDA) R37-DA0011796

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DIFFERENCES IN THE PROFILE OF NEONATAL ABSTINENCE SYNDROME SIGNS IN METHADONE- VS. BUPRENORPHINE-EXPOSED INFANTS.

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Aims: Methadone is the standard of care for the treatment of opioid dependence during pregnancy, but is associated with a neonatal abstinence syndrome (NAS) that often requires treatment and extended hospitalization. Studies indicate that infants exposed to buprenorphine in utero require less medication to treat NAS and have a shorter hospital stay compared to methadone-exposed infants. However, the extent to which prenatal exposure to methadone or buprenorphine results in a differential profile of NAS signs, perhaps leading to more favorable clinical outcomes in buprenorphine-exposed neonates, is unknown.
Methods: The profile of individual signs of NAS in methadone- vs. buprenorphine-exposed infants was compared using MOTHER study data. Participants were 129 infants born to opioid-dependent women who had been randomly assigned to receive either methadone or buprenorphine during pregnancy. Infants (methadone=72, buprenorphine=57) were assessed regularly for the first 240h postnatal using a 19-item modified Finnegan Scale. Analyses included scores of infants who were never treated and scores of treated infants up to the point of morphine-treatment initiation.
Results: Results suggest that the profile of NAS signs is different in buprenorphine- vs. methadone-exposed infants, with significantly greater incidence on some signs among buprenorphine-exposed infants (stuffiness, sneezing, loose stools), but significantly greater severity on a number of signs among methadone-exposed infants (disturbed and undisturbed tremors, hyperactive Moro reflex, excessive irritability, failure to thrive). Treatment initiation was also significantly later among buprenorphine-exposed neonates.
Conclusions: These results may help explain the more favorable clinical outcomes often observed in buprenorphine- vs. methadone-exposed infants.
Financial Support: NIDA RO1DA15738, 15764, 15778, 15832, 17513, 18410, & 18417

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USING ECOLOGICAL MOMENTARY ASSESSMENT TO PREDICT NEXT DAY METHAMPHETAMINE USE.

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Aims: The variables that lead to relapse in methamphetamine-dependent individuals are poorly understood but could be useful for improving behavioral interventions and resource allocation.
Methods: In this 9-week experiment, we used a random forest classifier to analyze the relationships between next day self-report methamphetamine (MA) use and daily ecological momentary assessments (e.g., stress, craving, withdrawal, and affect) in MA-dependent participants who were receiving manual-based psychosocial treatment and modafinil/placebo.
Results: Daily assessment completion did not predict same day or next day MA use (p=0.14, p=0.63 respectively). The resulting random forest classifier predicted next-day use with 73% accuracy (sensitivity 0.67, specificity 0.78, AUC(ROC) 0.80). The most predictive variables were craving visual analog score, PANAS positive affect subscale, and the strong and mild desires subscales of the Desires for Speed Questionnaire.
Conclusions: These results extend past reports that craving predicts relapse in MA abusers and indicate that fluctuating states, including stress and withdrawal, may play a role in relapse in MA dependence. Ecological momentary assessments of these states makes it possible to identify when individuals are at elevated risk of relapse and enable more effective treatment.
Financial Support: Supported by DA018179

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SENSORY REINFORCEMENT AS A PREDICTOR OF COCAINE SELF-ADMINISTRATION IN RATS.

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Aims: Locomotor response to novelty (LRN) has been found to predict acquisition of drug self-administration (SA), and has been hypothesized to be a rodent equivalent of sensation seeking (Dellu et al., Person. Ind. Diff., 4, 411-418, 1993). Sensation seeking is a personality trait indicated by preference for novel sensations and experiences. In humans, high scores on sensation seeking scales are associated with greater likelihood of drug abuse. We hypothesize that sensory reinforcement, operationally defined as operant responding to produce a novel visual stimulus (NVSR), indicates sensation seeking in rodents. Previous results suggest that LRN and NVSR are mediated by similar underlying behavioral processes (Gancarz et al., CPDD, 2009). Here, we evaluate the hypothesis that NVSR predicts acquisition of cocaine (COC) SA. The main goal of the proposed experiment is to determine the strength of association between NVSR and COC SA.
Methods: The reinforcing effects of a sensory reinforcer (5 s light onset) were tested. Rats were habituated to dark operant chambers for 10 days. Following habituation, a response contingent visual stimulus was available according to a variable interval 2 minute schedule of reinforcement. The rats were also tested for LRN by placing the rats in novel locomotor chambers for 1 hour. Finally, rats were implanted with chronic indwelling jugular catheters and tested for acquisition of COC SA for 10 days. During SA, snout pokes to the active side produced an intravenous infusion of 0.3 mg/kg COC (in the absence of any cues) according to a FR1 schedule of reinforcement followed by a 1 min time-out period.
Results: Preliminary results (n = 15) indicate there was a significant association between performance on NVSR and acquisition of COC SA ($r = 0.56$, $p < 0.05$). The experiment is currently ongoing; results for greater than 40 subjects will be reported.
Conclusions: These finding are consistent with the hypothesis responding to produce a sensory reinforcer is a measure of sensation seeking that predicts cocaine SA in rodents.
Financial Support: DA01058 AND DA026600

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EFFECTS OF SMOKING ON CAFFEINE INTAKE AMONG INDIVIDUALS WITH AND WITHOUT SCHIZOPHRENIA.

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Aims: Smoking induces the cytochrome P450 isoenzyme CYP1A2, which impacts caffeine metabolism. Therefore, understanding the higher caffeine intake among individuals with schizophrenia (SCZ) as compared to non-psychiatric controls (CON) requires examining this effect in smokers.
Methods: Secondary data analysis was performed on 142 smokers (68, SCZ; 74, CON) to assess 24-hour self-reported dietary caffeine intake and serum caffeine levels on a usual smoking day. Dietary intake was obtained from an adapted version of the caffeine consumption questionnaire. Assays for serum caffeine were conducted at the Clinical Pharmacology Laboratory at the University of California, San Francisco.
Results: No significant differences were observed between SCZ and CON, with respect to number of cigarettes per day (22.0 vs. 21; NSS) and dietary caffeine intake (374.0 vs. 257.0 mg; NSS). However, serum caffeine level were significantly higher for SCZ compared to CON (2175 vs. 1421 ng/mL; p=0.006). Although dietary caffeine intake was significantly correlated with daily smoking rate in both SCZ and CON, serum caffeine was only significantly correlated with daily smoking rate in SCZ and not in CON. Additionally, serum caffeine levels were not different among SCZ taking atleast one antipsychotic medication metabolized through CYP1A2 as compared to those taking antipsychotic medication metabolized through other pathways, suggesting no 1A2 inhibition by these medications.
Conclusions: Smokers with SCZ have higher serum caffeine levels compared to control smokers with similar smoking behavior. This may be attributed to higher caffeine intake among smokers with schizophrenia, but our findings suggest that self-reported dietary caffeine intake questionnaires may be unreliable for this population. Future smoking studies in schizophrenia should consider the confounding effects of caffeine. In addition, studies of obesity, diet and weight gain in schizophrenia should also include examination of both cigarette smoking and caffeine intake.
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CONTINGENCY MANAGEMENT FOR COCAINE ADDICTS: NEUROPSYCHOLOGICAL OUTCOMES.

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Aims: Results from a series of randomized clinical trials carried out in the USA and in Spain support the efficacy of the Community Reinforcement Approach (CRA) combined with a contingency management (CM) program (Budney & Higgins,1998) for improving treatment retention and cocaine abstinence in the treatment of cocaine addiction. Furthermore, a great number of studies have observed impairments on executive functions of cocaine addicts, but remains unclear whether these neuropsychological alterations improve when abstinence is achieved. The aim of the present study was to explore if the efficacy of CRA plus vouchers in retention and abstinence is reproduced in neuropsychological functioning.
Methods: Participants were twenty-four abstinent cocaine addicts that completed 12 months of treatment in one of two outpatient programs for cocaine dependence in Spain: CRA plus vouchers and CRA. A neuropsychological assessment protocol including different executive functioning measures was administered to participants at 12-month follow up. Urine specimens were collected throughout the treatment to monitor abstinence. Comparisons between groups were made using 2-sample t tests and $\chi 2$ tests.
Results: In the CRA plus vouchers group, mean percentage of cocaine-negative samples during treatment was 96.16% versus 92.24% in the CRA group. With regard to differences in neuropsychological functioning between groups at 12 months, those in the CRA plus vouchers had better scores in inhibitory control tasks. In particular, the number of corrected errors in the Go/No Go task was lower in the voucher group [p=.02]. There was also a trend for the voucher group to have better scores on fluency tests, though it was not statistically significant.
Conclusions: Combining CRA with CM improves treatment outcomes in cocaine-dependent outpatients. Knowledge of executive-control impairments may be clinically useful, but future studies should examine their possible rehabilitation with different interventions for cocaine addiction.
Financial Support: Spanish National Plan on Drugs (MSC-06-01) and the University of Oviedo (UNOV-08-PF).

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IS VIRTUAL REALITY THE BEST APPROACH FOR CUE EXPOSURE TREATMENT?

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Aims: Cue Exposure Treatment (CET) consists of controlled and repeated exposure to drug-related stimuli in order to reduce the associate craving. Virtual Reality (VR) has proven to be a promising tool for exposition in several psychopathological disorders, including substance use disorders. However, identifying which variables can modulate the efficacy of this technique is essential to select the most appropriate exposure modality. The aim of this study was to assess the relation between several individual variables and self-reported craving in smokers exposed to VR environments.
Methods: Forty-six smokers were exposed to 8 complex virtual scenes that reproduce typical situations where people urge to smokes. Craving was selected as the criterion variable and it was assessed during the exposure through a visual analogical scale from 0 to 100. Three types of variables were selected as the predictor variables: a) related to nicotine dependence (number of cigarettes per day, Fagerström test score and CO levels); b) related to anxiety (STAI-S and STAI-R scores); c) related to the sense of "being" in the virtual environments (Presence questionnaire score).
Results: The results show that the Presence questionnaire was the best predictor of the subjects' scores on the craving scale in most virtual environments. No variable related to nicotine dependence either anxiety were able to predict craving scores.
Conclusions: Virtual Reality technology can be very helpful for improving CET for substance use disorders. However, the use of virtual environments would make sense as long as the presence sense variable was high. Otherwise, the effectiveness of exposure might be affected.
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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PREDICTORS OF THERAPIST TURNOVER AND COMPETENCE IN AN EVIDENCE-BASED PRACTICE: FINDINGS FROM A LARGE-SCALE DISSEMINATION AND IMPLEMENTATION INITIATIVE.

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Aims: Training and turnover of staff are issues of importance for virtually all organizations, yet these issues have received only limited research attention within the field of substance abuse treatment. The primary aim of the current study was to examine the extent to which therapist characteristics and attitudes measured at an initial training workshop were related to therapist turnover and evidence-based practice (EBP) competence status.
Methods: Turnover (Employed/Not Employed) and EBP-Competence (EBP-Competent/Not EBP-Competent) status was assessed for 121 therapists at three different time points (6-, 9-, and 12-months post-training workshop). Using multilevel multinomial logistic regression analysis, therapist characteristics (e.g., age, race, gender) and work-related attitudes (e.g., job satisfaction, director leadership) were examined as predictors of therapists' transitioning from their initial default status (Employed/Not EBP-Competent) to the other statuses (e.g., Employed/EBP-Competent, Not Employed/Not EBP-Competent).
Results: Being male (OR=3.77), working for an agency with higher program needs (OR=1.19), and having poorer director leadership (OR=0.91) were the best predictors of transitioning to the Not Employed/Not EBP-Competent status. Reporting greater pressures for change (OR = 1.13), less months in position (OR=0.96), and less organization influence (OR=0.85) were found to be the best predictors of transitioning to the Employed/EBP-Competent status.
Conclusions: Given the current data suggests that therapists with greater experience and influence had more difficult obtaining EBP-Competence these individuals may require additional and/or different training assistance. Additionally, reducing program needs and improving director leadership appear to be two areas that organizations could address and might help improve the retention of well qualified therapists.
Financial Support: NIAAA (AA017625), NIDA (DA030462), and CSAT (HHSS270200700004C)

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RECREATIONAL DRUGS MODULATE THE DISCRIMINATIVE STIMULUS EFFECTS OF LSD.

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Aims: Lysergic acid diethylamide (LSD) is commonly used recreationally with a variety of other compounds, but little is known about how these compounds alter the effects of LSD. This study examines the effects of commonly used recreational drugs nicotine, ethanol, cocaine and methamphetamine on the discriminative stimulus effects of LSD.
Methods: Male Sprague-Dawley rats were trained to discriminate LSD, cocaine or methamphetamine from vehicle (0.9% saline) using a two-lever choice methodology. Nicotine, ethanol, cocaine and methamphetamine were tested alone or in combination with LSD in LSD-trained rats, and LSD was tested alone or in combination in cocaine- and methamphetamine-trained rats.
Results: Nicotine and cocaine produced intermediate levels of LSD-appropriate responding, but at doses which markedly decreased rates of responding. Similarly, LSD produced 54% methamphetamine-appropriate responding. Cocaine and methamphetamine produced small increases in the discriminative stimulus effects of low doses of LSD. In addition, LSD increased the effects of intermediate doses of methamphetamine. Nicotine and ethanol did not alter the discriminative stimulus effects of LSD.
Conclusions: Some compounds commonly co-abused with LSD slightly increase the discriminative stimulus effects of LSD, but also suppress response rates. The motivation for taking these compounds with LSD is not clear.
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RANDOMIZED CONTROLLED TRIAL OF A BRIEF CANNABIS INTERVENTION DELIVERED BY TELEPHONE.

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Aims: Despite the widespread use of cannabis relatively few cannabis users present to treatment. Study regarding the barriers to cannabis treatment highlights the importance of providing additional outpatient treatments that are specific to cannabis. This study explores the potential of the Cannabis Information and Helpline (CIH), a free national telephone service, to deliver a brief intervention to those seeking assistance with cannabis related problems in Australia.
Methods: To date 150 callers to the CIH have been randomised into two groups. The first group received a four session motivational enhancement and cognitive behavioural therapy treatment with a primary focus on reducing the participants' cannabis use over approximately four weeks. This group was assessed pre-treatment, post-treatment and at two months post treatment. The second group is a delayed treatment control condition and was assessed at similar time intervals to the intervention group. Preliminary results are available for 80 participants who have completed both follow up interviews.
Results: The current sample is mostly (70%) male, a mean of 36 years of age and commonly (55%) educated beyond secondary school. Cannabis use was significantly reduced at follow up for both groups, with no significant between group differences. However, reported confidence in reducing use was significantly greater at follow up for the intervention group compared to control.
Conclusions: This first study of an Australian cannabis helpline adds to research highlighting the utility of telephone counseling in settings outside of mental health. Despite study limitations, the reductions in cannabis use observed are comparable with face to face treatments.
Financial Support: This study was funded by the Australian Government Department of Health and Ageing

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CHARACTERIZATION OF THE EXTRACELLULAR VESTIBULE OF THE HUMAN SEROTONIN TRANSPORTER.

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Aims: To identify serotonin transporter (SERT) vestibular pocket amino acid residues important for recognition of transport inhibitors, via molecular modeling and site-directed mutagenesis.
Methods: Established SERT inhibitors were docked into a LeuTAa-based comparative SERT model to identify amino acids important for ligand binding. The docking poses guided targeting of side chains for mutagenesis; the point mutations created include W103A, V489F, K490T, E493D, E494H and E494T. Naïve N2A cells were transiently transfected with wildtype (WT) or mutant SERT cDNAs, and ligand binding and substrate transport capacities of each mutant were assessed. The structurally-dissimilar SERT inhibitors citalopram, sertraline, and cocaine displaced [^{125}I]RTI-55 or [^{3}H]-serotonin in binding or uptake inhibition assays, to yield K_i or IC_{50} values (GraphPad 5), respectively. Bmax values approximated extent of SERT mutant surface expression.
Results: SSRI binding affinities were significantly decreased for the E493D mutation; citalopram binding affinity decreased at E494T and E494H SERT. Binding affinity for cocaine decreased for V489F and E493D SERT. Regarding serotonin transport, sertraline displayed a significant decrease in uptake inhibition potency at E493D SERT. Contrastingly, the uptake inhibition potency of citalopram increased at E493D as well as at E494H, but decreased at W103A, and V489F SERT.
Conclusions: Consistent with recent reports, only modest effects on recognition of classic SERT inhibitors were detected from mutagenesis of selected extracellular vestibule residues. The findings served to elaborate details of the vestibule, but considering that the mutated residues were suggested by a SERT molecular model, refinement of the model is in order. A more mature SERT model should predict ligand binding sites and screen candidate ligands from small molecule structural databases.
Financial Support: R01DA026530, R01DA027806, P116Z050331, P116Z080180

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HEPATITIS C AMONG HOMELESS CLIENTS OF HEALTH CARE FOR THE HOMELESS PRIMARY CARE CLINICS.

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Aims: To describe the prevalence of and risk factors for hepatitis C virus (HCV) among homeless adults using eight Health Care for the Homeless (HCH) clinics nationally.
Methods: Data were collected for 387 participants through blood draws, structured interviews, and chart reviews.
Results: Overall prevalence of HCV-antibody positivity was 31.0%, including 70.0% among injection drug users and 15.5% among reported non-injectors. Much HCV infection was "hidden" as the majority (53.3%) of HCV-antibody positive participants were unaware of their status. Independent risk factors for HCV among the total sample included injection drug use, prison and tattoos; among injectors, risk factors included prison and ≥ 3 years of injection drug use; and among reported non-injectors, risk factors included tattoos and prison.
Conclusions: These HCH clinics serve high concentrations of HCV-infected injectors, making these and similar clinics priority intervention sites for aggressive screening, testing, education, and treatment for HCV and other blood-borne diseases.
Financial Support: Bureau of Primary Health Care, HRSA

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ACUTE TOLERANCE TO CHLORDIAZEPOXIDE QUALITATIVELY CHANGES THE INTERACTION BETWEEN FLUMAZENIL AND PREGNANOLONE IN RHESUS MONKEYS DISCRIMINATING MIDAZOLAM.

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Aims: Although positive $GABA_A$ modulators produce similar acute behavioral effects, actions at distinct binding sites on $GABA_A$ receptors confer differences between benzodiazepines and neuroactive steroids, including the development of tolerance to benzodiazepines and not cross tolerance to neuroactive steroids. Because changes in sensitivity differ depending on the site of action of positive $GABA_A$ modulators, interactions between drugs acting at different binding sites might be expected to change in tolerant subjects.
Methods: Four monkeys discriminated 0.178 mg/kg of the benzodiazepine midazolam while responding under a fixed-ratio 10 schedule of stimulus-shock termination.
Results: Positive modulators acting at benzodiazepine or neuroactive steroid sites (midazolam and pregnanolone, respectively) produced ≥80% responding on the midazolam lever. Flumazenil, which acts at benzodiazepine sites, antagonized midazolam and enhanced the midazolam-like effects of pregnanolone. When 10 mg/kg of the benzodiazepine chlordiazepoxide was administered 46 hr before sessions, the potency of midazolam decreased 3-fold (tolerance) whereas the potency of pregnanolone was unchanged. A dose of 0.1 mg/kg of flumazenil, which produced a 2-fold shift to the left in the pregnanolone dose-effect curve in otherwise untreated monkeys, shifted the pregnanolone dose-effect curve 2-fold to the right in monkeys that received chlordiazepoxide 46 hr earlier.
Conclusions: Thus, acute cross tolerance develops to a benzodiazepine and not to a neuroactive steroid in monkeys receiving a single dose of chlordiazepoxide, and in these tolerant monkeys, the interaction between flumazenil and pregnanolone is qualitatively different from their interaction in untreated monkeys, perhaps indicating that cross tolerance also develops to flumazenil.
Financial Support: Supported by USPHS grant DA09157 and DA17918 (CPF).

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FUNCTIONAL CONNECTIVITY OF INSULA CORTEX IN HUMAN ADOLESCENT SMOKERS AND NON-SMOKERS.

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Aims: Recent neuropsychological evidence suggests that the insula is crucial for regulating the urge to smoke cigarettes. This region likely regulates drug taking behavior in conjunction with other functionally connected regions; however, few studies have examined insular functional connectivity with respect to cigarette dependence. This relationship is particularly important to explore in adolescents given their vulnerability to nicotine dependence. Thus, we aimed to compare insula functional connectivity in adolescent smokers and non-smokers, hypothesizing that the groups would show differential strengths in connectivity.
Methods: We performed functional connectivity analysis on resting state fMRI data from late adolescent smokers (N=24) and non-smokers (N=25) using three insular seed regions: ventral anterior, dorsal anterior, and posterior. We correlated activation from the regions with whole brain activation and compared correlation maps across groups.
Results: The dorsal anterior insula showed greater functional connectivity with ventral temporal and occipital regions in non-smokers than smokers (whole-brain corrected). At uncorrected thresholds, all three regions showed greater connectivity with dorsal anterior cingulate/supplementary motor area and supramarginal/postcentral gyri in non-smokers than smokers (P<.001). No regions showed greater connectivity with the insula for smokers versus non-smokers.
Conclusions: These results show that insular functional connectivity is decreased in adolescent smokers, suggesting under-recruitment of functional circuitry connected to the insula. Such deficits may contribute to smoking maintenance in adolescence that often endures through adulthood.
Financial Support: Phillip Morris USA, endowments from the Katherine K. & Thomas P. Pike Chair in Addiction Studies, and the Marjorie Green Family Trust (EDL)

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PREVALENCE, SOURCES, MOTIVATIONS AND DIVERSION OF PSYCHOACTIVE PRESCRIPTION MEDICATIONS AMONG A UNIVERSITY SAMPLE IN LEBANON.

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Aims: Nonmedical use of psychoactive prescription medications is a worldwide public health concern. Data from the Western world illustrates a significant rise in youth, but remains scant and anecdotal in the Arab region despite the medications' growing popularity, ease of access, and misperceived low risk. An exploratory study was conducted in a sample of university students in Lebanon to examine the prevalence and patterns of medical and non-medical use of the most commonly abused classes of prescription drugs.
Methods: An IRB-approved cross-sectional study was conducted on a sample of 573 undergraduate and graduate students at the American University of Beirut (AUB). Proportionate cluster sampling ensured representation of all Faculties. Data was collected using a self-filled anonymous questionnaire.
Results: About 30% of students reported medical use and 16% admitted to non-medical use of any psychoactive prescription drug in the past year. Pain medications were the most commonly used both medically and non-medically (12-month prevalence: 20% and 10%, respectively), in both genders. Family members and health professionals were the primary reported sources. Diversion occured in 20% of the ever medical users. Motivation for use was predominantly for the intended purpose yet varied by source (e.g., illicit reasons if friend/partner and/or illegal drug dealer, and therapeutic purpose if family/healthcare professional). Across all medications, 33-63% of students perceived it easy/very easy to obtain medications if they wanted to.
Conclusions: Findings suggest that a considerable proportion of youth in Lebanon may be self-medicating themselves without any supervision or follow-up, despite a few illicit users. The study highlights the need for a larger more representative study, and calls upon not only restricting sales without prescription, but also increasing awareness among parents and doctors, and even patients.
Financial Support: American University of Beirut (University Research Board) seed grant

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NIDA CTN ELECTRONIC MEDICAL RECORDS PROJECT: IMPLICATION OF ADOPTING STANDARDIZED CORE DATA ELEMENTS IN HEALTH IT SYSTEMS OF DRUG-ABUSE TREATMENT PROVIDERS.

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Aims: There is an urgent need within the substance-use-disorders (SUD) treatment field to develop and implement consensus-based common core data elements (CDEs) with standardized vocabularies relevant to drug addiction treatment that could be incorporated and widely adopted into harmonized electronic medical record systems (EMRs). This will benefit patients by improving the quality of care and will assist in integration of specialty addiction treatment into disciplines of mainstream medicine.
Methods: To achieve these aims, the NIDA Clinical Trials Network (CTN) has collected and collated dozens of treatment-form-related information and standardized instruments to develop a treatment-relevant set of CDEs. We refined these CDEs following a consensus-based meeting of federal, state, and community-based treatment stakeholders and providers. The framework for this process will be explained with a collaborative "Mind Map" for developing and implementing core questions as CDEs for EMRs on SUD in primary care and SUD specialty treatment settings. Key branches of the map include: 1) involving stakeholders in development of consensus-based CDEs, 2) choosing brief screening questions and instruments, 3) collaboratively developing a data collection hierarchy and core questions as CDEs, and 4) considering interoperability requirements for "Certified EHR Technology" and CMS requirements for "Meaningful Use".
Conclusions: Current progress will be provided in developing EMR core questions as CDEs for use in primary care and SUD specialty treatment settings. Implications of this project for the future of drug addiction treatment will be discussed. NIDA is especially interested in input from CPDD members on data collection hierarchy and core data elements, and on the overall strategy in regards to other sources of input, other stakeholders who should be consulted, and other "next steps" as we move forward.
Financial Support: NIDA

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DIFFERENCES IN ENVIRONMENTAL ENRICHMENT PREDICT SELF-ADMINISTRATION OF A LOW UNIT DOSE OF METHYLPHENIDATE IN RATS.

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Aims: Environmental enrichment (EE) during development has previously been shown to reduce rates of drug self-administration of psychostimulants in preclinical models of drug use. Additionally, recent data from our lab suggests that EE protects against escalation of cocaine self-administration at low unit doses using an extended access model. It is unclear, however, if EE protects against methylphenidate (MPH) self-administration. Despite its abuse potential in both humans and non-humans, MPH is widely prescribed for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). The current study examined the effects of EE on acquisition of MPH self-administration, as well as determination of a MPH dose-effect function.
Methods: Rats were raised from 21 days in an enriched condition (EC) with social cohorts and novel objects, a social condition (SC), with only social cohorts, or in an isolated condition (IC) without social cohorts or novel objects. At 51 days of age, rats were then trained to self-administer MPH (0.3 mg/kg/infusion) on a fixed ratio schedule of reinforcement. During the next phase of the experiment, subjects were exposed to 0.056 mg/kg/infusion, 0.1 mg/kg/infusion, 0.56 mg/kg/infusion, and 1.0 mg/kg/infusion MPH in either ascending or descending order. All subjects were then exposed to saline self-administration for seven consecutive sessions.
Results: When assessed in young adulthood, there were no differences in MPH acquisition; however, IC rats self-administered significantly more saline and MPH (0.056 mg/kg/infusion) than both EC and SC rats during the dose-effect determination phase.
Conclusions: Results suggest that EE protects against MPH self-administration at a low unit dose, but this protective effect may be surmountable with a higher dose.
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ASSOCIATION OF BULIMIA NERVOSA WITH TREATMENT OUTCOMES OF METHAMPHETAMINE-DEPENDENT ADULTS.

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Aims: Although weight loss is among the most commonly cited reasons for using methamphetamine (MA), little is known about the association between eating disorders and treatment outcomes in this population.
Methods: Using data from 526 adults in the largest psychosocial clinical trial of MA users conducted to date, this study examined psychiatric, substance use, and functional outcomes of MA users with bulimia nervosa 3 years after treatment.
Results: Bulimia nervosa was observed among 2.4% (N=13) of the participants and was associated with poorer MA use outcomes, increased health service utilization, and higher levels of functional impairment across a number of domains.
Conclusions: Addressing MA use among adults with eating disorders may be helpful as a means of facilitating better treatment outcomes.
Financial Support: The research presented herein was supported by NIDA Grant 1K23DA020085 awarded to S. Glasner-Edwards and by the Methamphetamine Abuse Treatment – Special Studies (MAT-SS) contract 270-01-7089 and grants numbers TI 11440–01, TI 11427–01, TI 11425–01, TI 11443–01, TI 11484–01, TI 11441–01, TI 11410–01 and TI 11411–01, provided by the Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration (SAMHSA), US Department of Heath and Human Services.

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WITHDRAWN

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CHRONIC MARIJUANA USE IS ASSOCIATED WITH GENDER-DEPENDENT ALTERATIONS IN CORTICAL MICRO-STRUCTURE.

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Aims: Marijuana (MJ) is the most widely used illicit drug in the world and chronic use has been associated with memory deficits. Diffusion tensor imaging (DTI) can assess micro-structural changes in the brain. We hypothesized that chronic adult MJ users would show micro-structural alterations in brain regions associated with language and working memory. We also evaluated for gender-dependent alterations in these brain regions.
Methods: 25 controls (15 males & 10 females; mean age: males 27.5+2.7 y, females 24.0+1.2 y) and 25 MJ users (15 males & 10 females; mean age: males 26.1+2.1 y, females 22.6+1.0 y; mean age of first use: males 15.5+0.8 y, females 16.5+0.6 y; mean daily cannabis use: males 4.8+1.9 g/day, females 3.1+0.9 g/day; mean duration MJ use: males 10.1+2.3 y, females 10.7+6.1 y; all had positive urine for THC) were evaluated. DTI was performed on a 3 T Siemens Trio scanner using axial spin-echo EPI DTI scans with full-brain coverage (12-diffusion-directions). DtiStudio version 3.0.1beta was used to calculate fractional anisotropy, mean diffusion (ADC), axial and radial diffusivities. Automated ROI analyses using Large Deformation Diffeomorphic Metric Mapping were performed in 65 bilateral regions. Data were analyzed using a 2-between (Drug Use & Gender) 1-within (Hemisphere) mixed model ANOVA.
Results: MJ users had lower radial diffusivity than controls in middle frontal gyri ($p=0.02$). In addition, male MJ users had lower ADC in angular gyri ($p=0.002$), and lower axial diffusivity in superior occipital gyri ($p=0.02$), compared to male controls. Female MJ users had similar diffusion metrics with female controls.
Conclusions: As predicted, we found micro-structural abnormalities in language and working memory brain regions of MJ users. Lower diffusivity suggests more compact axonal fibers, which may result from altered neural development. Male MJ users appear to be more susceptible to these alterations than female users.
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INHIBITORY CONTROL INDEXES EARLY-IN-TREATMENT ABSTINENCE AMONG OPIOID-DEPENDENT YOUNG ADULTS TREATED WITH BUPRENORPHINE.

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Aims: To determine in young adults with opioid dependence the extent that control over behavior, as measured in a task requiring inhibition of an impulsive action (anti-saccade), contributes to initiation of abstinence after the first week of treatment with buprenorphine as part of an ongoing study.
Methods: Forty treatment-seeking, opioid dependent young adults (M= 23 yrs, SD= 2.3) were inducted onto buprenorphine 16mg/day the prior week. Participants were predominately Caucasian (92.5%), male (62%) and were high school graduates or higher (90%). Initial assessments included the severity of dependence scale (SDS), opioid withdrawal scales, heroin Tiffany craving scale and anti-saccade performance. All participants reported weekly drug use on a TLFB and provided urine samples for drug testing.
Results: The subjects were dependent on opioids (heroin or opioid analgesics) for an average of 1.9 years and 65% used intranasal opioid analgesic. One patient was excluded from analysis because of incomplete trials on the anti-saccade task. Inhibitory control significantly correlated ($r = 0.42$, $p < 0.006$) with levels of abstinence. Inhibitory control ($t = 3.73$, $p < 0.004$) and severity of dependence ($t = 2.62$, $p < 0.02$) were significantly predictive of levels of abstinence, whereas craving ($t < 1$) and opioid withdrawal ($t = 1.5$) were not.
Conclusions: Inhibitory control and SDS were successful predictors of levels of abstinence during the initial phase of buprenorphine treatment. Given these preliminary results, it may be possible to predict overall outcome prior to treatment and identify individuals who may require treatment enhancement for successful outcome.
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EXECUTIVE COGNITIVE DYSFUNCTION IN RATS WITH A HISTORY OF ETHANOL DEPENDENCE.

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Aims: Disturbances in executive functions are a key element of the self-regulatory failures characteristic of alcohol and drug abuse. However, to date, little is known about how separate processes of executive functioning are altered in drug addiction. The purpose of this study was to investigate the consequences of alcohol dependence on different components of executive functions, such as cognitive flexibility and behavioral disinhibition, by using two tests: strategy set-shifting and differential reinforcement of low rates of responding.
Methods: Whereas the strategy set-shifting test measures a type of cognitive flexibility that implies inhibition of a previously relevant strategy and activation of a newly optimal strategy, the differential reinforcement of low rates of responding (DRL) task is thought to measure "impulsive action" (or behavioral disinhibition) by "delay responding". In experiment 1, male Wistar rats were trained to lever press for water on a DRL 40 seconds schedule of reinforcement. Once stable responding was achieved, rats were made ethanol dependent by intragastrically administering alcohol (20% w/v) for 5 consecutive days in a total volume of 22 ml/kg/day, and then tested again in the DRL 40s task. In experiment 2, a new group of male Wistar rats were initially made dependent via intragastric ethanol intubation (as in experiment 1). Then, they were trained in a visual discrimination learning task, and finally tested in a response-strategy discrimination test, which required disengagement from a previously relevant visual-cue strategy used in the former learning task.
Results: No significant differences in impulsive action were found between dependent and non-dependent rats. For the strategy set-shifting task, although both alcohol-treated and non-alcohol treated rats' performance in the learning task was similar, alcohol-dependent rats showed a deficit on response conflict in the set-shifting phase.
Conclusions: These findings suggest that the capacity to modify ongoing strategies in response to changing environmental contingencies might be compromised by a history of ethanol dependence.
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TEN YEARS OF REGIONAL INEQUALITIES IN DEATHS BY DIAGNOSIS OF MENTAL AND BEHAVIORAL DISORDERS DUE TO PSYCHOACTIVE SUBSTANCE USE: A VIEW OF THE BRAZILIAN PUBLIC HEALTH DATA.

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Aims: To compare inequalities related to deaths by mental and behavioral disorders due to psychoactive substance use in the geographical regions of Brazil, from 1999 to 2008, and to analyze trends of deaths by type of substance used.
Methods: Study based on secondary data from the Mortality Information System of the Ministry of Health and data from the National Household Sample Survey of 2008. Data were generated through the register of underlying causes of death in municipalities and death certificates, coded according to ICD10. Data of per capita income correspond to the average number of minimum wages received by person, stratified according to categories defined by the Brazilian Institute of Geography and Statistics. The death coefficient was calculated according to sex, age, schooling, marital status and per capita income. Trends were analyzed by region and type of substance used.
Results: 61,513 deaths were analyzed - 75.7% of the total deaths from mental and behavioral disorders occurring in Brazil, yielding an average of 3.44 deaths per 100,000 inhabitants. We found inequalities in alcohol use trends: there is an increasing ratio of deaths in all regions, most significantly in the Northeast (where 14.8% of the population receives up to 0.74 times the minimum wage) and less in the South (9.4% of the population with 0.75 to 1.99 times the minimum wage), but the greater death coefficient increase was in North (12.7% up to 0.74 times the minimum wage). Inequalities in tobacco use refer to the increasing trend in South, married men and multiple drugs use in the Midwest.
Conclusions: Although regional differences may be associated with better data collection in the wealthier regions of the country, our results point to increasing trends in using alcohol, tobacco and multiple drugs in all regions (r2=0.9016). Brazil still needs to enforce specific local policies to minimize the regional differences.
Financial Support: There is no financial support.

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CANNABIS WITHDRAWAL SYNDROME IN DSM-V.

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Aims: There are no accepted diagnostic criteria for cannabis withdrawal syndrome (CWS). This study evaluated diagnostic criteria for CWS proposed in DSM-V.
Methods: 469 adult, non-treatment-seeking cannabis smokers provided retrospective self-report data on their "most difficult" quit attempt without formal treatment. Prevalence, time of onset, and peak intensity (5-point Likert scale) for 40 withdrawal symptoms (drawn from the literature) were assessed via computer-administered questionnaire. Subject groups were compared using chi-square or ANOVA. Symptom clustering was evaluated with principal components analysis (PCA).
Results: Subjects were [mean (SD)] 27.7 (9.1) years old at the start of their index quit attempt and had been using cannabis at least weekly for 11.3 (8.8) years. 65.2% averaged daily smoking over the 6 months prior to quitting. 41.2% met proposed DSM-V criteria for CWS. There were no associations with sex, race, age, or type of cannabis preparation used. There were significant positive associations between amount or frequency of cannabis use prior to the quit attempt and experiencing CWS. Subjects with CWS were significantly more likely to relapse during their quit attempt (92.8% vs. 83.3%) and had a shorter duration of abstinence (median 60.8 days vs. 91.2 days). Alternative syndromal criteria (dropping physical symptoms from DSM-V list; requiring > 2, > 3, or > 4 symptoms from a list of 11) yielded a similar prevalence of CWS and similar associations with prior cannabis use and relapse. The PCA yielded 11 factors, including some symptom clusters not included in DSM-V.
Conclusions: Findings support the concurrent and predictive validity of the proposed DSM-V withdrawal syndrome, but suggest that the list of withdrawal symptoms and number required for diagnosis warrant further evaluation.
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NEUROIMAGING HEAVY CANNABIS USERS VS. SPORADIC AND NON-USERS: WORKING MEMORY AND DECISION-MAKING.

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Aims: Cannabis is the most commonly used illegal drug in most countries and progression into use of other illegal drugs (ecstasy, cocaine) is frequently observed regardless of the legal repercussions. Few investigations, however, have addressed the role of neurocognitive functions on the trajectory of cannabis and other drug use. In this prospective study, brain function activity during working-memory and decision-making were assessed with fMRI.
Methods: Heavy cannabis users (n=20), a sporadic cannabis users group (n=33) and a cannabis naïve control group (n=22) were included (average age: 21.9, IQ: 109, no differences on age and IQ between the groups). fMRI analyses were performed using FSL (cluster restriction Z>2.3 and corrected cluster sign. threshold p=.05).
Results: Analyses of the fMRI working memory task (N-back) indicated lower activity in the cingulate gyrus, parahippocampal gyrus and precuneus in heavy cannabis users compared to sporadic users and controls, indicating lower ability to recruit working-memory areas when memory load increases. fMRI results of decision-making (Iowa Gambling Task) indicated that heavy cannabis users had less signal change between wins and losses in the inferior prefrontal cortex and anterior cingulate, indicating diminished sensitivity to rewards and losses.
Conclusions: These results show that even in a subclinical group of heavy cannabis users functional brain abnormalities are present. This indicates that heavy cannabis use in the absence of cannabis dependence is related to diminished functional brain activity during working memory and abnormal reward processing (decision-making task). Follow-up data on changes in cannabis and other drug use, will be complete June '111, and will be related to functional brain activity.
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SWAY: A NEW GENETIC MODEL FOR DIMINISHED COCAINE-REINFORCED BEHAVIOR.

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Aims: Sway is genetic trait that arose spontaneously during selective breeding of rats for decreased intravenous drug self-administration. Rats with this abnormality exhibit a specific form of tremor that causes them to move from side-to-side as they walk, which develops in the late childhood without a generalized decline in brain function. The purpose of these experiments was to examine different effects of cocaine in rats carrying the Sway trait.
Methods: Rats exhibiting the Sway trait were crossed with randomly bred Wistar rats and directly observed for gait abnormalities. All other behavioral analyses were conducted in younger rats, prior to the onset of changes in gait. Locomotor activity was quantified by infrared beam interruption, as rats received injections of saline or intraperitoneal cocaine (7.5 mg/kg per injection). Rats acquired self-administration of 0.32 mg/kg per injection of cocaine under FR-1 (each lever-pressing response causes an injection of cocaine), and were subsequently allowed to self-administer 0.1, 0.2, or 0.4 mg/kg per injection under FR-5 (cocaine is delivered after 5 lever-presses).
Results: The Sway trait was inherited as an autosomal recessive pattern with incomplete penetrance within the Wistar strain. Cocaine- but not saline- induced locomotor activity was decreased in rats that were either heterozygous or homozygous for the Sway trait, with no differences in cocaine-induced conditioned-place preference observed. In rats homozygous for Sway, self-administration of low-dose cocaine was diminished, with no changes observed for higher doses of cocaine.
Conclusions: In summary, Sway is a unique genetic model that causes reductions in cocaine-induced locomotor activity and cocaine-reinforced behavior during early development. These changes occur prior to gait abnormalities that develop during late childhood. Effects on gait are readily observed, which should allow mapping of the specific mutation that gives rise to the Sway trait.
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 ATYPICAL ANTIDEPRESSANT MIRTAZAPINE ATTENUATES THE EXPRESSION OF MORPHINE-INDUCED PLACE PREFERENCE.

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Aims: Despite FDA-approval of multiple pharmacotherapies aimed at maintaining abstinence in opioid-dependent patients, opioid abuse remains prevalent. We recently revealed that the atypical antidepressant mirtazapine attenuates methamphetamine-seeking in rats (Graves & Napier, Biolog Psych '10; Herrold et al., Drug Alcoh Depend '09). We sought to expand these findings to determine the ability of mirtazapine to attenuate morphine-induced place preference and expression of motor sensitization.

Methods: Rats were conditioned using an 8 day conditioning paradigm wherein morphine injections (10mg/kg; ip) were paired in one chamber of a 3 chamber conditioned place preference apparatus (Accuscan Instr, Columbus, OH). Saline was paired on alternate days with the opposite chamber. Rats were tested for place preference on day 10 with either a 30min or 24hr pretreatment of mirtazapine (5.0mg/kg) or vehicle. On day 11 a subset of rats were tested for the expression of motor sensitization to a 5.0mg/kg morphine challenge with a 30min pretreatment of either mirtazapine (5.0mg/kg) or vehicle.

Results: Rats developed morphine-induced place preference with four, once-daily pairings which was attenuated by a 30min but not 24hr pretreatment of mirtazapine. Rats developed and expressed motor sensitization to morphine which was attenuated by a 30min pretreatment of mirtazapine (horizontal and vertical/rearing activity).

Conclusions: Mirtazapine shows strong promise as substance abuse pharmacotherapy for methamphetamine and we now extend these findings to include morphine. Mirtazapine is an approved antidepressant that antagonizes NEα2, histamine1, and 5-HT2A/2C/3 receptors with inverse agonist effects at constitutively active 5-HT2C receptors (Chanrion et al., Mol Pharm '08). While mirtazapine could be readily repurposed in the clinic, further efforts are needed to elucidate the mechanism(s) of action that underlies its ability to antagonize both stimulants and opiates.

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PREDICTING SUBSTANCE USE AMONG CHILDREN WITH ADHD: CLINICAL UTILITY OF IMPAIRMENT INDICES.

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Aims: ADHD is the most commonly diagnosed disorder among children and has long been associated with increased risk of substance use disorders (SUD), and the same is true for ODD/CD (Iacono et al., 2008; Zucker, 2006). However, recent conceptualizations have suggested that DSM diagnoses used alone may not be as useful for exploring risk for SUD compared to environmental risk factors such as school functioning and peer relationships (Iacono et al., 2008). The goal of the current study was to examine the extent to which childhood ADHD, ODD/CD symptoms and impairment across key domains of risk (academic and peer relations) predict substance use in later adolescence and early adulthood.

Methods: Participants (n=364, Mean age=17, range 11-28) were recruited from individuals diagnosed as children with ADHD-age at initial evaluation: ranged 5-16 yrs w/90% < 12 yrs. Parent and teacher reports of ADHD/ODD/CD symptoms were collected during the baseline evaluation along with measures of social, educational, and family risk. Academic impairment was assessed via a standardized achievement test. The primary follow-up outcome data were frequency and initiation of substance use (alcohol, cigarettes, and marijuana were aggregated) obtained through interview.

Results: Regression analyses indicated that childhood symptoms of ADHD (B=-.22, $p<.01$) but not ODD/CD predicted initiation of substance use. Problems with peers also predicted initiation of substance use (B=-.24, $p<.001$). In terms of academic impairment, findings indicated that adolescents/young adults who reported never using any substances had higher achievement scores in childhood compared to adolescents/young adults who reported using substances, $F=4.08$, $p<.05$.

Conclusions: These findings highlight the clinical utility of impairment ratings/indices and show that among children with ADHD, environmental risk factors in peer and academic functioning incrementally contribute to a risk for earlier substance use initiation in adolescence and early adulthood.

Financial Support: This research was supported by grants from NIAAA, NIDA, NIMH, and NIEHS.

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HETEROGENEITY IN TREATMENT RESPONSE FOR COCAINE DEPENDENCE: A BAYESIAN SUB-GROUP ANALYSIS INCORPORATING HISTORICAL DATA.

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Aims: In cocaine users, baseline, comorbid drug use has consistently predicted treatment outcome in general, and for some medications specifically. This study examined the moderating effects of baseline marijuana use on response to levodopa/carbidopa in a clinical trial for cocaine dependence. Bayesian modeling with informative prior distributions based on historical data provided a probabilistic measure of evidence for subgroup effects.

Methods: Two completed studies provided the samples for the historical dataset (Study 1: n = 39 levodopa; n = 40 placebo), and current dataset (Study 2: n = 53 levodopa, n = 58 placebo): subsets of the overall trial data, selected due to their comparability in dosing for levodopa: 800/200 mg and 400/100 mg b.i.d.

Results: There was a high probability (0.96) that baseline marijuana use predicts differential response to treatment with levodopa/carbidopa. Simple effects indicate that for participants receiving levodopa/carbidopa versus placebo the probability that baseline marijuana use confers harm in terms of treatment outcome is 0.981 versus 0.172 respectively. For every additional day of marijuana use reported at baseline, participants in the levodopa/carbidopa condition demonstrated a 5% decrease in Treatment Effectiveness Score (TES) (R.R. 0.95, 95% C.B.I. 0.86-1.07) compared to a 5% increase in TES (R.R. 1.05, 95% C.B.I. 1.00-1.12) among placebo participants.

Conclusions: Bayesian, subgroup analyses with informative priors permit consideration of historical evidence in characterizing heterogeneity in response to treatment. In the current context this points, with high probability, to the existence of a subgroup effect of baseline marijuana use on response to treatment for cocaine dependence with levodopa/carbidopa. Specifically, higher marijuana use predicts poorer outcomes in the levodopa/carbidopa condition, but not in the placebo condition.

Financial Support: NIDA 2-P50-DA009262

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ADAPTING STANDARDIZED RESEARCH INSTRUMENTS TO MATCH A RURAL NATIVE AMERICAN COMMUNITY'S EXPERIENCE: BUILDING THE BASE.

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Aims: Good research design for clinical trials should include a period of careful consideration of the instruments that will appropriately measure change. Research instruments have not been adequately validated with Native Americans, and often do not capture the experience of Native American communities or the outcomes that would interest them. We describe the process of choosing and adapting research measures in a rural reservation community for a randomized controlled trial of Treatment as Usual versus an adapted evidence-based outpatient substance use disorder treatment.

Methods: The research instruments were chosen to be sensitive to variables that should change with treatment, including substance use and consequences, abstinence self-efficacy, and psychological distress. The next step involved choosing measures that would capture community-specific variables such as cultural identity, spirituality, and discrimination. The University-based researchers searched the research literature to identify measures that might capture important constructs. The selected instruments underwent several revisions to reflect community experiences. This process was collaborative and based on community input from the Tribal Council, local staff, and cultural educators. The final instruments were approved by the Tribal Council and piloted with nine participants.

Conclusions: Allowing time for careful instrument selection and adaptation improves the quality of research and data with Native American populations, and provides an opportunity to build community-university relationships. Researchers should report on reliability of measures adapted and tested in Native American communities to add to the sparse literature. Choosing instruments in a collaborative manner ensures that the research outcomes will be meaningful to the community itself.

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UNEMPLOYMENT, CLIENT EMPLOYMENT STATUS, AND SUBSTANCE ABUSE TREATMENT OUTCOMES IN NEVADA.

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Aims: The rapid increase in statewide unemployment in Nevada from 5% in 2006 to 14% in 2010 provided an opportunity to examine the relationships between statewide unemployment, client employment status and substance abuse treatment outcomes. We assessed the following issues: 1.Client employment status at treatment admission. 2. Length of stay (LOS) in treatment. 3. Treatment completion with abstinence. 4. Association of low versus high statewide unemployment with these factors.
Methods: Substance abuse treatment admission in Nevada (N=29,207 clients) was assessed during periods of low unemployment (5%, 7/2006-12/2007, N=12,894) and high unemployment (14%, 1/2008-2/2010, N=16,313). First, clients' employment status, and other client characteristics were compared by unemployment level. Next, survival analyses examined predictors of length of stay (LOS), both overall and separately by treatment modality . Finally, ordinal logistic regression analysis examined potential predictors of client status at discharge within each period: 1. Completed treatment with abstinence (N=3,272), 2. Completed but not abstinent (N=5,602), 3. Did not complete (N=8573), and 4. Transferred/In jail (N=6,820).
Results: Client unemployment at admission rose with higher state unemployment (45.3% vs. 60.5%), while full-time employment fell (25.3% vs. 11.3%), respectively. LOS was significantly shorter for unemployed compared to full-time employed clients (N=9,183, OR=1.21, p=.000 during high unemployment vs. N=5,366, OR=1.051, p=.042 during low unemployment). Compared to working full-time (N=4,736), the odds of completing treatment with abstinence was significantly lower for clients working part-time, (N=1,652, OR=.578), unemployed (N=12,984, OR=.642), or out of-the labor force (N=4895, OR=.642, P=.000), respectively.
Conclusions: Substance abuse treatment outcomes are associated with State unemployment levels. The extent to which these are causally related requires further study.
Financial Support: None.

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THE WOMEN'S RECOVERY GROUP STUDY: CHALLENGES AND STRATEGIES FOR THERAPIST TRAINING, ADHERENCE AND SUBJECT RECRUITMENT IN A 2-SITE GROUP THERAPY TRIAL.

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Aims: The WRG study is a 2-site Stage II clinical trial comparing 12-sessions of a new manual-based group treatment for women with substance use disorders with mixed-gender Group Drug Counseling (GDC). 90 women were randomized to WRG (N=45) or mixed-gender GDC (N=45), with 45 men assigned to GDC. The study is designed to be consistent with usual community practice and implemented in an open enrollment format, posing challenges to study implementation, especially in therapist training/adherence and subject recruitment/retention. The current analysis describes strategies developed to facilitate implementing this mixed efficacy/effectiveness trial of open-enrollment substance abuse group therapy.
Methods: The following challenges were identified: (1) training and transition of therapists at two study sites to maximize adherence; (2) recruitment, enrollment, and retention of subjects in open enrollment groups; (3) maintenance of subject enrollment to ensure gender balance and an adequate flow of subjects to maintain group participant numbers.
Results: The study team implemented several strategies. For therapist training, 2 teams of therapists trained simultaneously. Team 1 therapists conducted groups months 1-12; team 2 therapists received booster training at month 11, overlapped with team 1 therapists during month 12, and conducted groups months 13-25. Adherence was measured with weekly supervision and ratings. To maintain adequate group numbers, boosted recruitment and enrollment of subjects was necessary, and strategies included enhanced advertising, referral incentives for clinicians, and strategies to shorten time from baseline assessment to group enrollment.
Conclusions: Open-enrollment group therapy trials present specific challenges to therapist training and adherence, as well as subject recruitment, enrollment, and retention. Specific strategies can facilitate implementation of such mixed efficacy/effectiveness trials.
Financial Support: 2R01DA15434 from NIDA

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EFFECT OF CONTINGENCY MANAGEMENT ANALOGS ON COCAINE BEHAVIORAL ECONOMIC DEMAND IN THE LABORATORY SETTING.

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Aims: Behavioral mechanisms underlying the efficacy of contingency management (CM) are incompletely understood. We are studying analogs of CM in cocaine abusers to determine whether higher- vs. lower-magnitude predictable and probabilistic money reinforcement increases cocaine elasticity, and whether cocaine demand is functionally equivalent at similar unit prices comprised of differing progressive ratio/unit dose combinations.
Methods: The study uses a two-factor (2 Cocaine Unit Dose [5 and 10 mg intranasal] X 5 Money Alternative), within-subject, randomized crossover design. In the two predictable reinforcement conditions ($1 and $3 per choice), completed money choices always earn these amounts (100% probability; monetary/voucher CM analogs). Three probabilistic conditions are yoked for expected utility to the high predictable amount ($3) condition. In these probabilistic conditions, each money choice earns a lottery draw (prize CM analogs): High ($6 with 50% probability), Medium ($12 with 25% probability) and Low ($24 with 12.5% probability). All earned money is delivered after all sessions are completed.
Results: Preliminary analyses (n=9 completed) show that cocaine elasticity varies significantly across contingency conditions, $F(5,77)=18.75$, $p<.0001$. Relative to the absence of a money alternative, 100% certainty of earning $1 and $3 produces 3.2- and 9.9-fold increases in normalized cocaine demand elasticity (Pmax values = 1280, 396 and 129) across unit doses, which are functionally equivalent. Demand curves for probabilistic conditions (Pmax values = 231, 214 and 417 for $6 [50%], $12 [25%] and $24 [12.5%]) are more inelastic than the $3 predictable condition, i.e. subjects are discounting probabilistic amounts.
Conclusions: Given that delay to money reinforcement is constant across conditions, these data suggest that predictable non-drug reinforcement increases cocaine elasticity more than matched-magnitude probabilistic reinforcement. These findings may have implications for designing CM treatment approaches.
Financial Support: Supported by NIH R01 DA026861 and Joe Young, Sr. Funds (State of Michigan)

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GENDER DIFFERENCES IN 30-YEAR TRAJECTORIES OF HEROIN AND OTHER DRUG USE AND HEALTH OUTCOMES.

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Aims: To examine gender differences in 30-year trajectories of heroin and other drug use among individuals who were in methadone maintenance treatment in California in the early 1980s and their health outcomes.
Methods: We followed-up individuals who were originally sampled from methadone maintenance treatment records and interviewed in 1978-1981 as participants in a baseline study (N=914). Nearly half (n=428; 46.8%) of the original study sample was deceased. Of the remaining 486 subjects, 343 completed a follow-up interview in 2005-09 (70.6% of non-deceased). Longitudinal natural history data was obtained on their drug use, treatment participation, and legal status over the 30-year period as well as their current health status and functioning. Close to half (46.9%) of the follow-up sample was female and the average age was 58.2 (SD=4.9) years for males and 54.9 (SD=3.7) years for females. Trajectory group modeling was used to identify distinctive trajectory groups based on monthly probabilities of heroin and other drug use; group differences were examined on sociodemographic and background characteristics obtained at the baseline interview.
Results: Four distinct heroin-use trajectory groups were identified. A greater proportion of women (60%) were in the "rapid decrease" group (odds of heroin use < 10% by 10 years after initiation) and a greater proportion of men (54%) were in the "no decrease group" (odds of heroin use > 90% over the 30-year period). The "rapid decrease" group had higher rates of alcohol and amphetamine use over time. More school problems and earlier ages of heroin initiation and first arrest were associated with more persistent heroin use. Women had significantly more chronic health problems than men and poorer physical and mental health compared with women in the general population (using age and race/ethnicity based norms).
Conclusions: Childhood antecedents of heroin-use trajectories were identified in this longitudinal study as well as gender differences in patterns of heroin and other drug use over time and in current health status and functioning.
Financial Support: Supported by the NIDA grants DA015390 and P30 DA016383-06

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ESTIMATING TREATMENT EFFECTS IN THE PRESENCE OF DIFFERENTIAL FOLLOW-UP BETWEEN GROUPS.

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Aims: We set out to evaluate the effectiveness of an evidence-supported adolescent substance abuse treatment program (MET/CBT5) as delivered by community-based treatment providers (CBTPs) relative to its performance in a controlled research trial (CRT). However, follow-up rates in the CBTPs were extremely low (40%) compared to the CRT (98%). Thus, we developed a new tool for assessing the sensitivity of findings on treatment effectiveness to differential follow-up in the treatment programs being compared.
Methods: We hypothesized that our findings in favor of youth in CBTPs might be reversed to favor youth in CRT if youth who were more likely to be lost to follow-up had outcomes that were at least 0.25 effect sizes worse than those who were followed-up in the CBTPs. To assess this, we randomly censored youth in the CRT such that probability of censoring depended on the client's outcome at follow-up in order to make the CRT group have the same follow-up rate as the CBTPs. We re-fit our propensity score models and outcome analyses with this reduced sample of CRT participants. We varied the magnitude of the relationship between the outcome and probability of being follow-up to determine how differential the mean outcome would need to be in the followed-up and not followed-up youth before our observed results were likely to differ.
Results: Primary analyses signaled that CBTPs performed comparably, if not superior to, CRT. The sensitivity analysis indicated that these treatment effect estimates were sensitive to assumptions about differential follow-up. However, a strong association (i.e, effect size differences in outcomes greater than 0.60 between those followed-up and those not) would be required to completely reverse our findings and favor outcomes in CRT over CBTPs.
Conclusions: The method developed is a promising tool for assessing sensitivity of treatment effectiveness studies to differential follow-up. Evidence from this study suggests that MET/CBT5 has been successfully transported into CBTPs.
Financial Support: DA017507-04A

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PSILOCYBIN DOSE-EFFECTS: ASCENDING DOSE SEQUENCE ASSOCIATED WITH GREATER PERSISTING POSITIVE EFFECTS AT HIGHER DOSES.

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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 persisting positive changes in attitudes, moods, and behaviors. The present study characterized the effects of a range of psilocybin doses tested in an ascending or descending dose sequence.
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-hour 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. During sessions volunteers wore eyeshades and directed their attention inward.
Results: On post-session questionnaires assessing somatic, psychological, and mystical-type experience, psilocybin effects were an increasing function of dose, with no effect of dose sequence. Four weeks after each session volunteers completed a questionnaire rating persisting effects. In addition to showing monotonically increasing dose effects, all six positive subscales (attitudes about life, attitudes about self, mood, altruism, behavior, and spirituality) showed significant Dose x Dose Sequence interactions. Inspection of these data showed that this effect was due to the ascending dose sequence producing relatively larger effects at the 20 and 30 mg/70 kg doses and relatively smaller effects at lower doses compared to the descending sequence.
Conclusions: Psilocybin produces dose-related increases in acute effects and persisting positive effects of hallucinogens. The ascending dose sequence was associated with relatively greater positive persisting effects than the descending dose sequence, suggesting that prior exposure to lower doses may facilitate the positive effects of high doses. An implication for studies of possible therapeutic effects of psilocybin is that exposure to lower doses should precede exposure to a high dose.
Financial Support: DA003889; Council on Spiritual Practices; Heffter Research Institute; Betsy Gordon Foundation

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MARIJUANA AND MOOD: A ROLE IN BIPOLAR DISORDER.

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Aims: Individuals with co-occurring bipolar disorder (BPD) and substance abuse often experience poor treatment response, relapse of mood symptoms and a variety of psychosocial difficulties. While the precise reasons for comorbidity remain unknown, some studies of bipolar patients report that substance use is directly related to at least one symptom, commonly depression or racing thoughts, and that the majority of patients report symptom improvement as a result of the substance use. As marijuana (MJ) is commonly used by patients with BPD, we examined the impact of MJ use on mood symptoms in MJ-smoking bipolar patients (MJBP; N=10) and pure MJ smokers (MJ; N=18) in order to test the hypothesis that bipolar patients would experience improved mood symptoms after smoking MJ.
Methods: All subjects completed a series of clinical rating scales using a handheld PDA device three times daily and after episodes of smoking MJ, which included the POMS, MADRS, YMRS, and HAM-A. A difference score was calculated from pre-MJ rating scales as compared to post-MJ rating scales, which were completed within 4 hours of smoking MJ. T-tests for both within and between group differences on the change scores were computed.
Results: For each of the clinical scales, the MJBP group demonstrated significant improvement following smoking MJ relative to pre-MJ levels while the MJ group appeared to have a slight worsening of symptoms. Notably, total mood disturbance (TMD), a composite measure of the POMS, was reduced from 24.1 to 6.8 in the MJBP group (p=.0001) while it was increased from -3.40 to .70 in the pure MJ group (p=.025).
Conclusions: These pilot data suggest that MJBP subjects experience a significant improvement in mood symptoms after smoking MJ while pure MJ smokers exhibit a slight worsening of clinical state. Consistent with previous reports of BPD patients using drugs to improve mood related symptoms, these data underscore the likelihood that MJ may act as a mood stabilizer for patients with BPD and underscores the importance of examining MJ use and cannabinoid-based therapies.
Financial Support: NIDA R21 and R03 to Dr. Gruber

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RIFAMPIN, BUT NOT RIFABUTIN, TREATMENT MAY BE ASSOCIATED WITH OPIATE WITHDRAWAL IN BUPRENORPHINE MAINTENANCE THERAPY.

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Aims: Rifampin is a first-line drug in the treatment of tuberculosis and methicillin-resistant Staphylococcus aureus (MRSA). Rifampin is associated with opiate withdrawal symptoms in methadone-maintained individuals necessitating use of rifabutin as an alternative.
Methods: In this study, we determined whether a significant drug interaction would occur when buprenorphine and rifampin or rifabutin were administered simultaneously at standard clinical doses. Opioid-dependent individuals eligible for opioid replacement therapy participated. Buprenorphine (BUP)/naloxone (NLX)-maintained individuals (12 in the rifampin/buprenorphine study and 9 in the rifabutin/BUP study) participated in two 24 hour pharmacokinetics studies; the first following at least 2 weeks on a stable dose of BUP/NLX and the second following continued opioid therapy and up to 15 days of rifampin 600 mg daily or rifabutin 300 mg daily (standard clinical doses).
Results: Rifampin (p=0.02), but not rifabutin was associated with opiate withdrawal. BUP mean AUC was decreased 70% by rifampin (p<0.001) and 35% by rifabutin (p<0.001). Norbuprenorphine AUC was reduced 88% with concomitant rifampin administration (p<0.001), but rifabutin had no effect on this active metabolite. Those experiencing opiate withdrawal required BUP/NLX dose increases of 25-100% for up to 5 days, but these doses remained in the FDA-approved dose range. No clinically significant effect of BUP/NLX treatment on rifampin or rifabutin pharmacokinetics was observed.
Conclusions: Rifampin may be associated with opiate withdrawal requiring BUP/NLX dose increases in some opioid-dependent patients. Rifabutin is an alternative to rifampin in opioid dependent populations treated with BUP/NLX and requiring treatment for co-occurring tuberculosis or MRSA.
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THE RELATIONSHIP BETWEEN SERVICES DELIVERED AND SUBSTANCE USE OUTCOMES IN NEW MEXICO'S SCREENING, BRIEF INTERVENTION, REFERRAL AND TREATMENT INITIATIVE.

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Aims: Recent years have seen increased diffusion of SBIRT for substance use in various healthcare environments. This study examined the relationship between substance use outcomes and service variables within the SBIRT model as delivered in New Mexico's SBIRT program.

Methods: Over 55,000 adult patients were screened for substance misuse throughout New Mexico as part of the SBIRT Initiative. Among those who received services, a random subsample was selected for 6 month follow-up. This study used baseline, 6 month follow-up, and services data for adult participants in the New Mexico SBIRT evaluation (n=1,208). Mixed-effects Poisson models were used to examine changes in self-reported frequency of illicit drug use, alcohol use, and alcohol intoxication as a function of service level (Brief Intervention– BI vs. Brief Treatment/Referral to Treatment– BT/RT) and number of service sessions received.

Results: Participants reported decreased frequency of illicit drug use, alcohol use, and alcohol intoxication 6 months after receipt of SBIRT services ($p<.001$). Compared to those who received BI, participants who received BT/RT had sharper reductions in frequency of drinking ($p<.05$) and alcohol intoxication ($p<.05$). Number of service sessions was associated with reduced frequency of alcohol use ($p<.01$) and intoxication ($p<.01$), but only among those who received BI. The rate of change in illicit drug use did not differ significantly based on service variables.

Conclusions: In a real-world, multi-site rural SBIRT program, participants reported considerable decreases in frequency of substance use. Services of higher intensity were associated with greater magnitude of change in drinking behaviors, but not drug use. Future studies should identify the preferred mix of services in the SBIRT model as its use continues to expand.

Financial Support: Support from Center for Substance Abuse Treatment, SAMHSA (Grant TI 15958) and the National Institute on Drug Abuse (DA026003; PI: Robert P. Schwartz).

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PATIENT ACCESS TO BUPRENORPHINE TREATMENT IN APPALACHIA: A GEOGRAPHIC ASSESSMENT USING SAMHSA'S PHYSICIAN-LOCATOR WEBSITE.

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Aims: Opioid abuse poses a major public health problem in Appalachia, which spans 13 states. Program-based opioid dependence treatment availability is limited particularly in rural areas. Physicians waivered to prescribe buprenorphine for office-based opioid dependence treatment may list contact information on a SAMHSA physician-locator website, which is commonly searched by patients to access care. We used these listings to examine distribution of buprenorphine prescribers across Appalachia and determine whether prescribers are geographically less available in rural Appalachia.

Methods: Physicians were identified from the physician-locator website October 2010. Based on zip code, Appalachian county practice location was ascertained and urbanicity coded using 2003 Department of Agriculture Rural-Urban Continuum Codes (RUCC) based on population and metropolitan proximity: Metropolitan (Codes 1–3), Urban (Codes 4–7), Rural (Codes 8–9). Per capita physician distribution was determined using 2009 adult population estimates (18+yr) for each county and descriptively analyzed.

Results: The 1025 physicians in Appalachian counties were located in Alabama (n=127), Georgia (83), Kentucky (67), Maryland (24), Mississippi (16), North Carolina (63), New York (31), Ohio (54), Pennsylvania (268), South Carolina (33), Tennessee (128), Virginia (20), West Virginia (111). The total adult population for all counties, 19.3 million, yielded an overall per capita physician-availability rate of 5.3 MDs/100,000 Appalachian adults. State rates ranged from 3/100k (Mississippi, Ohio) to 12/100k (Maryland). Physician availability was similar by urbanicity, ranging from 3-7 MDs/100k across all nine RUCC codes.

Conclusions: Based on opioid dependence prevalence and limited specialty care availability, these findings indicate inadequate buprenorphine prescriber availability throughout Appalachia, not only in rural, non-metropolitan regions. The results will inform health policy and indicate a need for physician outreach efforts to hopefully improve treatment access.

Financial Support: Supported by K23 DA020000

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THE SEROTONIN (5-HT) AND ESTROGEN RECEPTOR SYSTEMS DYNAMICALLY INTERACT TO REGULATE SEROTONIN TRANSPORTER ACTIVITY.

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Aims: Dysregulation of serotonin neurotransmission, including alterations in 5-HT receptors and transporter (SERT), contributes to the etiology of psychiatric disorders, including vulnerability to drug addiction. Fluctuations of ovarian estrogenic hormones during cycling, pregnancy vs. the postpartum period, menopause, and post-menopause are associated with mood disorders and perhaps with different success rates among women undergoing treatment for drug addictions. Estradiol (E2) reduces 5-HT uptake via the SERT. Either direct interactions between estrogen receptor beta (ERβ) and SERT, and/or shared intracellular signaling pathways may be involved. The purpose of this study was to investigate the interactions between the 5-HT2R family (5-HT2AR, 5-HT2CR) and ERβ mechanisms, and the potential functional consequence of E2-mediated regulation of ERs, 5-HT2Rs or SERT expression and function in a neuronal cell line (RN46A).

Methods: Membranes from RN46A cells (derived from embryonic dorsal raphe neurons) were isolated by differential centrifugation. Membrane-enriched protein fractions were separated by SDS-PAGE, transferred to PVDF membranes and analyzed by immunoblot. ERβ, SERT, 5-HT2AR and 5-HT2CR were detected using rabbit polyclonal (Santa Cruz; H-150), mouse monoclonal (Santa Cruz; 24A5), rabbit polyclonal (Neuromics; RA24288), and mouse (Santa Cruz, D-12) antibodies, respectively.

Results: We detected immunoreactive bands corresponding to the ERβ (MW = 56 KDa), SERT (MW = 70 KDa) and 5-HT2CR (MW = 46 KDa) in RN46A cell membranes.

Conclusions: These data indicate that ERβ, 5-HT2CR, and SERT are expressed in membrane fractions of RN46A cells. We are now primed to investigate the protein:protein interactions between these proteins to elucidate the functional consequences of these interactions.

Financial Support: DA020087, DA024157

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AMPHETAMINE-OPIOID INTERACTIONS IN THE HUMAN BRAIN REWARD SYSTEM—A PET STUDY USING [11C]CARFENTANIL.

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Aims: There is ample evidence for the involvement of the opioid system in stimulant dependence. For instance, in both animal and human laboratory studies the opioid antagonist naltrexone attenuates several of the effects of amphetamine. The aim of this study was to investigate the acute effects of amphetamine on the brain opioid system for the first time in humans.

Our hypothesis was that an acute intravenous dose of amphetamine as compared to placebo would cause an endogenous opioid release in the human brain reward system, measurable as a reduction of the binding potential for the mu-opioid receptor radioligand [11C]carfentanil.

Methods: 10 healthy young men were investigated with [11C]carfentanil PET in three sessions: at baseline, after placebo and after an intravenous amphetamine dose of 0.3 mg/kg bodyweight. The order of amphetamine and placebo was double-blind and randomized. PET scans were performed with a Siemens HRRT system. Data were analyzed with SPM5 using the simplified reference tissue model, applying manually drawn regions of interest for every subject.

Results: There were no significant differences in [11C]carfentanil binding potential between amphetamine and placebo conditions in any of the investigated brain regions.

Paired t-tests and ANOVA were used to assess differences between amphetamine, placebo and baseline conditions.

Conclusions: An acute, intravenous dose of amphetamine does not appear to cause an endogenous opioid release in healthy subjects. The role of the opioid system in amphetamine dependence needs to be further investigated in a chronic model of the disease.

Financial Support: Swedish Research Council

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N-ACETYL-CYSTEINE ALTERS DRUG-CUE ENHANCED SUBJECTIVE EFFECTS OF SMOKED METHAMPHETAMINE IN METH-DEPENDENT VOLUNTEERS.

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Aims: N-acetyl-cysteine (NAC) is a pro-drug for cysteine, which is a substrate for the glutamate/cysteine antiporter. This antiporter exchanges cysteine for glutamate, increasing synaptic glutamate levels. Preclinical studies show that restoring accumbal glutamate blocks reinstatement of drug-seeking. NAC also decreases craving and use in cocaine-dependent volunteers. Here we examined whether NAC treatment altered the reinforcing and subjective effects of smoked METH in METH-dependent volunteers and whether NAC influences subjective measures related to drug-cues paired with smoking METH.
Methods: This ongoing study uses a within-subjects (n=5), randomized, placebo-controlled, double-blind design. Participants (PTs) receive NAC (0, 1800, 3600 mg, PO, given in divided doses) for 5 days. On Days 1-3 PTs are exposed to active cue video showing METH consumption or neutral nature scene cues. On Days 4 and 5 PTs are exposed to active or neutral cues, and receive METH or placebo (PLB). PTs must pay $5 if they choose METH.
Results: PTs chose METH significantly more than PLB($p<0.01$). METH "HIGH" was rated greater during exposure to METH cues vs. neutral cues. NAC dose-dependently decreased cue-enhancement of METH "HIGH". The highest dose of NAC (3600mg) tended to decrease METH ratings of "DESIRE". Further ongoing data acquisition will determine statistical significance of these findings.
Conclusions: Consistent with previous studies in patients with cocaine dependence, our results indicate that NAC attenuates the subjective ("HIGH") and drug-associated cue effects ("DESIRE" i.e. craving) but not the reinforcing effects of smoked METH.
Financial Support: NIDA:5R21DA0-024756-02, NEWTON

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DEMOGRAPHIC AND SEX-RELATED FACTORS ASSOCIATED WITH 4 DRUG USE BEHAVIORS IN WOMEN AT RISK FOR HIV.

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Aims: To identify associations among demographic, sex- and drug- related risk behaviors in women at risk for HIV.
Methods: Demographic characteristics and sexual practices were related to past 90 day IDU, sex with an IDU and crack use as well as "high" during last sex act for N=1091 women enrolled in 3-site HIV risk reduction trial. Analyses included Chi Square, ANOVA and binary logistic regression.
Results: Women were 34 yo, 58% Black, 24% Hispanic and 18% White; 41% did not complete HS, 72% were unemployed and 61% were unstably housed. Three-fourths (74%)were "straight", 45% ever-married and 87% ever-pregnant. During the preceeding 90 days, they averaged 2.8 sex partners, with M=1.7 sexual encounters per week (89% without a condom); 81% had a primary partner. IDU (24%) was associated with age, race (White), unemployment, trading sex for drugs/money and sex with same-day-met and HIV/STI infected partners. Sex with an IDU (14%)also was associated with age, race (White), trading sex for money/drugs and sex with infected partners as well as less education, unstable housing, having a main partner, non-monogamous partners and never-condom use. Crack use was related to race (Black), unstable housing, unemployment, pregnancy, trading sex for drugs/money and having more and non-monogamous partners. Finally, "high" during last sex act (35%)was related to age, sexual orientation, unemployment, trading sex for money/drugs, more and non-monogamous, same-day-met and infected partners.
Conclusions: As expected, demographic and sex-related risk behaviors were associated with targeted drug-risk behaviors. While considerable overlap was found, each drug-related risk behavior had unique correlates that characterized a sub-set of women at risk for HIV. For instance, women who had sex with IDUs engaged in more self-defeating behaviors with high risk partners and did not use condoms. In contrast, crack users were black, unstably housed mothers. Research is needed to define subgroups of women at risk for HIV so that risk reduction inteventions can be tailored to their needs.
Financial Support: CMHS:#1UID SM 52070

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EFFECT OF TOBACCO CIGARETTE SMOKING ON MARIJUANA WITHDRAWAL AND RELAPSE.

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Aims: Under controlled laboratory conditions, daily marijuana smokers who smoke tobacco cigarettes are 10x more likely than non-tobacco smokers to relapse to marijuana use after 3 days of marijuana abstinence. The objective of this within-subject study was to determine whether cessation of cigarette smoking decreased marijuana relapse relative to smoking as usual.
Methods: There were 2 inpatient phases: a Quit phase and a Smoking-as-Usual (SAU) phase, presented in counter-balanced order. We used contingency management procedures to foster tobacco cessation prior to the Quit phase. On the first inpatient day, participants smoked experimenter-administered, active marijuana (5.5% THC). For the next 3 days, inactive marijuana (0.0% THC) was available for self-administration (abstinence), followed by 4 days when 5.5% THC was available for self-administration (relapse). Participants purchased self-administered marijuana using study earnings.
Results: Non-treatment seeking, daily marijuana (9 marijuana cigarettes/day) and cigarette (10/day) smokers (13M; 2F) completed the study. Almost all participants relapsed to active marijuana (86-93%), and there was no effect of phase on rates of relapse. However, placebo marijuana tended to be self-administered more during the Quit phase relative to SAU ($p < 0.06$). During active marijuana administration, ratings of hungry and sedated were greater during the Quit phase relative to SAU. During marijuana abstinence, mood was significantly worse during the Quit phase relative to SAU, e.g., increased ratings of angry, tired, depressed, and jittery.
Conclusions: Direct nicotine effects do not appear to mediate the positive association between cigarette smoking and marijuana relapse. Perhaps factors intrinsic to those who smoke both cigarettes and marijuana (e.g., impulsivity, stress reactivity, genetic polymorphisms) increase the likelihood of relapse rather than an effect of nicotine per se. These data suggest that tobacco cessation alone would not improve marijuana treatment outcome.
Financial Support: Supported by DA19239 and DA031005.

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FEELING LEFT OUT? PREDICTING THE BEHAVIORAL AND BRAIN RESPONSE TO SOCIAL STRESS.

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Aims: Social exclusion, being ignored groups of individuals in one's presence, is one of the most emotionally salient states in the human experience. Substance abusing populations, particularly women, are particularly vulnerable to social exclusion, which may contribute to drug abuse, dependence and relapse. This study aimed to determine whether baseline levels of belongingness, locus of control, and self esteem can predict the behavioral and brain response to social exclusion in cocaine users.
Methods: Before a functional MRI scan, male and female cocaine users (n=20) and healthy controls (n=25) performed a Need Threat Assessment which measures baseline sense of belongingness, self-esteem, locus of control, and a sense of meaningful existence. All participants were then told they would play "virtual catch" with two other individuals that were also in neighboring MRI scanners. During inclusion,players threw the ball to the participant frequently. During exclusion, players gradually stopped throwing the ball to the participant. A multiple linear regression model was used to determine whether the brain response to exclusion could be predicted by baseline measures of belongingness, self-esteem, locus of control, and meaningful existence. The Need Threat Assessment was repeated.
Results: At baseline cocaine users had a more external locus of control than controls, and a lower sense of belonging. A lower baseline sense of belonging was the best predictor of changes in the Need Threat Assessment as a result of social exclusion. It was also the strongest predictor of the brain response to exclusion. A lower sense of belonging was associated with higher activity in the extended amygdala, insula and cingulate cortex, regions also involved in drug craving and reward. These correlations were strongest in the female users.
Conclusions: These data suggest that we may be able to predict vulnerability to social stress, particularly in female addicts, by assessing baseline behavioral indicators such as belongingness and locus of control.
Financial Support: K01DA027756, DA20648, DA06634

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DEFINING TYPES OF OPIOID AND COCAINE USERS BASED ON LATENT CLASS ANALYSIS.

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Aims: Heroin and cocaine use made up over 30% of all drug use treatment entries in 2007 (SAMHSA, 2009). Both substances can be taken by various Routes of Administration (ROA's) that may be associated with unique risk factors. This study attempts to address an important gap in the literature by using a purely data-driven method, Latent Class Analysis (LCA), to identify specific patterns of polydrug use in this population.
Methods: PARTICIPANTS AND PROCEDURES
Baseline data from the Baltimore site of the NEURO-HIV study (Severtson et al., 2010) was used. Participants (N=504) who used cocaine and/or heroin in the past 6 months were recruited from the community. Participants received blood tests, gave urine samples tested for drug use and diseases including HCV, and completed semi-structured interviews.
DATA ANALYSIS
Only ROA's and substances with a past-month prevalence of 20% or higher (alcohol; cigarettes; injecting "speedball", i.e., cocaine and heroin mixed; injecting heroin; snorting heroin; injecting cocaine; smoking crack; and marijuana) were included as indicators in the LCA, as suggested by Monga et al, 2007. M-plus was used to generate models of the data. Latent class regression, using posterior probability-based multiple imputations (pseudo-class draws), was conducted to examine the relationship between the latent classes and HCV status.
Results: The BIC suggested that a 3-class model best fit the data. The prevalent indicators (having an estimated probability of 50% or greater within classes) are as follows: Class 1 ('non-injectors', n=223)- alcohol, cigarettes, snorting heroin, smoking crack; Class 2 ('heroin injectors', n=165)- cigarettes, injecting heroin; Class 3 ('dual injectors', n=116)- alcohol, cigarettes, injecting speedball, heroin, and cocaine. Heroin injectors (OR=6.8;95%CI:6.4-7.1) and dual injectors (OR=11.1;95%CI:10.5-11.7) were both over six times more likely to be positive for HCV than non-injectors.
Conclusions: The existence of these subgroups suggests a high need for targeted prevention and intervention efforts.
Financial Support: Supported by NIDA grants T32DA007292 and R01DA020929

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THC EFFECTS ON LOCOMOTOR ACTIVITY AND ELEVATED PLUS MAZE BEHAVIOR DURING DOSING AND DURING SPONTANEOUS WITHDRAWAL IN ADOLESCENT RATS.

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Aims: Due to the localization of cannabinoid receptors throughout the limbic system, striatum and cerebellum, stimulation by cannabinoids can alter anxiety and activity levels. Cannabinoid withdrawal may also disrupt behavior but this has not been well characterized in the animal literature. Aim: to examine the effects of chronic Delta9-tetrahydrocannabinol (THC, main psychoactive component in marijuana) on behavior during drug administration and spontaneous withdrawal in mid-adolescent male and female rats.
Methods: Male and female Sprague Dawley rats (8-14/group) were administered 2, 7.5 or 15mg/kg THC or vehicle (pluronic acid/saline) via intraperitoneal injection 1x daily from postnatal day 35-41, a period approximating early to mid adolescence in humans. Locomotor activity levels were measured for 1 hr immediately following injection on days 35, 38 and 41 during drug administration, and on days 42, 44, 47, 50, 53 and 56 during the withdrawal period. Elevated plus maze behavior was assessed on days 42, 44 and 56 during withdrawal.
Results: Locomotor activity results indicate dose-dependent locomotor depression in both males and females during the dosing period, an effect that persisted during withdrawal. 15 mg/kg THC significantly reduced the time spent in the center of the box in both males and females during drug administration, which might be considered an anxiogenic response, whereas in males 2mg/kg appeared to be anxiolytic. There were also long-term decreases in time spent in the center of the box on PND 56, suggesting THC has long-term anxiogenic effects. Analysis of elevated plus maze behavior also demonstrates differential effects of THC on time in the open arm of the maze and number of stretch postures, measures of anxiety.
Conclusions: THC produces dose-dependent effects on locomotor activity and anxiety-related behaviors during drug administration as well as during spontaneous withdrawal. Additionally, females show greater effects of THC on anxiety than males. Clearly cannabinoid administration during adolescence produces long-term effects on behavior.
Financial Support: NIH RO1 DA019348, P50 DA04584-01

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EXAMINING FASD TRAINING OF TRAINERS PARTICIPANTS' STIGMATIZING ATTITUDES TOWARD ALCOHOL USE IN WOMEN OF CHILDBEARING AGE.

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Aims: Examine attitudes toward alcohol use by women of childbearing age among substance abuse treatment professionals (Counselors) recruited to participate in an FASD Training of Trainers (TOT) event; Evaluate the impact of the TOT on those attitudes.
Methods: University of Nevada, Reno faculty members developed a TOT Curriculum based on the Centers for Disease Control and Prevention's FASD Competency-Based Curriculum Development Guide (2009). Pre/post-TOT attitudes were measured through the use of scenarios depicting women in various alcohol-related situations. Counselors who possessed effective training skills, an interest in FASDs, and/or working in women's substance abuse treatment programs were nominated by their regional ATTC to participate in the TOT.
Results: Twenty-one Counselors attended the TOT and completed pre/post surveys. Results showed significant decreases in stigmatizing attitudes towards alcohol use by women of childbearing age following the TOT. However, Counselors remained significantly more negative towards pregnant vs. non-pregnant alcohol dependent women (complete item-level analysis will be presented).
Conclusions: Results suggest that, despite the fact that participants work with individuals who have substance use disorders (SUDs), there may be a degree of stigma associated with the inability of a woman who has an SUD to stop drinking when she gets pregnant. The TOT was shown to effectively decrease stigmatizing attitudes. However, the data also suggest a need to educate Counselors' regarding addiction as a chronic relapsing brain disease. Including the neurobiological basis for addiction in the current TOT Curriculum would increase Counselors' knowledge as well decrease stigmatizing attitudes among individuals training the Curriculum to other Counselors, and is crucial to changing how individuals work with women of childbearing age who use alcohol or have SUDs.
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THE DEVELOPMENT OF METHAMPHETAMINE USE DISORDER IN A CLINICALLY ASCERTAINED LONGITUDINAL SAMPLE.

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Aims: To examine the development of methamphetamine (meth) use disorders in a sample of clinically ascertained adolescents who were followed up in young adulthood.
Methods: Structured interviews were administered at 2 time points to assess substance use among a clinical sample of adolescents (n=261) initially recruited from a substance use disorder (SUD) treatment program. 91% were males and 57% were white. Subjects were followed from adolescence (mean age=15.7, SD=1.2) into young adulthood (mean age=23.8, SD=2.7). Of those who reported having tried meth at least 5 times (n=132), those who developed a meth use disorder (n=97) at Wave 2 were compared to those who did not (n=35).
Results: Of the entire sample, at Wave 1, 35% had used meth and 20% had a meth use disorder. At Wave 2, 51% had used meth, 37% had a meth use disorder. Preliminary analyses show that those with meth use disorder started using meth sooner (age 15.8 vs. 16.9, F=4.2, p=.043), had a greater number of other SUD diagnoses (4 vs. 3, F=8.5, p=.004), and were more likely to have cannabis (χ2=5.7, p=.017) and hallucinogen use disorders (χ2=7.0, p=.008), but not other SUDs, than those who had not developed meth use disorder. However, the group that developed a meth use disorder did not show significantly higher DSM-IV Conduct Disorder symptoms or ADHD symptoms at Wave 1.
Conclusions: There is evidence that the development of meth use disorders begins in adolescence. Those who develop meth use disorders may show different substance use patterns than those who have non-meth SUDs, and any attentional or impulsive problems associated with meth use may result from, rather than precede, meth use.
Financial Support: P60DA011015, R01DA012845, R01DA021913, 1K01DA023487

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IMPAIRED SLEEP FUNCTIONING IN PRESCRIPTION OPIOID-DEPENDENT INDIVIDUALS.

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Aims: Nonmedical prescription opioid use is a significant and widespread societal problem that continues to rise. Sleep impairment has been indicated as a motive for nonmedical prescription opioid use (Boyd et al., 2006). Opioid use, however, is also associated with increased sleep dysfunction (Dimsdale et al., 2007). This study preliminarily examined sleep functioning in men and women with prescription opioid (PO) dependence (n=66) as compared to a healthy control group (n=41) enrolled in a larger, ongoing laboratory study of PO dependence and stress reactivity.
Methods: At the baseline visit, participants completed the Insomnia Severity Index (ISI; Morin, 1993), the Epworth Sleepiness Scale (ESS; Johns, 1991) and the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989).
Results: The findings revealed poorer sleep integrity and continuity among the PO group as compared to the control group, as evidenced by greater difficulty staying asleep (p = .000) and waking up too early (p = .000). Significantly greater latency to onset of sleep (45.4 min vs. 14.5 min; p<.001) was observed among the PO group, as well. The PO group evidenced significantly more dozing (p =.01) and disruption in daily functioning due to sleep impairment (p=.000), and tended to report greater inactivity (p = .07) during the day as compared to controls. Finally, the PO group was more likely to use other medications to aid in sleep (p <.001), and report more physical pain (p<.001), thermoregulation problems (p=.003) and nightmares (p=.003) than the control group.
Conclusions: While preliminary, these finding aid in describing and understanding a population in need of enhanced clinical care. Data collection is ongoing and data from the full sample will be reported.
Financial Support: Funding acknowledgement: NIDA grant K23 DA021228 (SEB)

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SMOKING RATES SIGNIFICANTLY ELEVATED IN DRUG-DEPENDENT STUDY POPULATIONS.

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Aims: Compare the rates of cigarette smoking in 1) marijuana, cocaine, alcohol, methamphetamine and prescription opiate dependent individuals participating in non-treatment seeking studies, and 2) the overall rate of smoking in the surrounding county.
Methods: Demographics data and smoking status were collected from healthy adults (age 18+) with alcohol, cocaine, marijuana, methamphetamine, or prescription opiate dependence participating in non-treatment research studies in South Carolina. Chi-Squared tests were used to compare smoking rates in participants with smoking rates in the general county (acquired from the Behavioral Risk Factor Surveillance System, 2000-2006).
Results: Participants demonstrated significantly higher smoking rates (p<.0001) than the baseline county smoking rates. The methamphetamine group (Pickens County) had a smoking rate of 88.4% compared to 24.0% county-wide smoking rate. The prescription opiate (84.6%), cocaine (83.3%), alcohol (50.5%) and marijuana (45.3%) groups (Charleston County) all smoked at significantly higher rates than the county-wide rate of 22.0%.
Conclusions: Despite declines in US smoking rates over the past several decades, widespread cigarette smoking persists, particularly among individuals with addictive disorders. In this study, non-treatment seeking substance dependent individuals smoked at rates 2 to almost 4 times higher than the general population. The findings emphasize the need for additional research and treatment of nicotine dependence in substance dependent populations.
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CANNABINOIDS INHIBIT T-CELLS IN AN IN VITRO ASSAY FOR GRAFT REJECTION, THE MIXED LYMPHOCYTE REACTION.

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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 previously shown that the cannabinoids delta9-tetrahydrocannabinol (THC) and anandamide are immunosuppressive for mouse spleen cells in the primary and secondary plaque-forming cell assays, via CB2, and that THC and CB2-selective agonists, JWH-015 and O-1966, inhibit the Mixed Lymphocyte Reaction (MLR). The present study sought to determine which cell type(s) are affected by the cannabinoids in the MLR, and to investigate possible mechanisms for their immunosuppressive action.
Methods: The MLR is considered to be an in vitro correlate of skin and organ transplant rejection. Cannabinoids might, therefore, be a candidate class of compounds to prolong graft survival in transplant patients. 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. Mouse spleen cells were separated by sorting with Flow Cytometry into CD3+ (T-cells), CD11b+ (monocytes, granulocytes, macrophages, and natural killer cells) and CD3-CD11b- fractions. CD3+ or CD11b+ fractions were treated with JWH-015 or O-1966 before being washed and added back to the untreated cell fractions and performing the MLR.
Results: Inhibition of the MLR only occurred when the CD3+ population was treated, and not when the CD11b+ population was treated. Furthermore, treatment with JWH-015 and O-1966 in the MLR resulted in decreased release of IL-2, a pro-inflammatory cytokine produced by T-cells.
Conclusions: These results provide additional support for the potential of cannabinoids as useful therapies to block graft rejection.
Financial Support: This work was supported by NIDA grants DA13429, DA06650, and T32-DA07237.

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VOUCHERS, PRIZES AND CLINIC PRIVILEGES AS REINFORCEMENT FOR ABSTINENCE: A REVIEW OF THE EFFICACY OF CONTINGENCY MANAGEMENT APPLICATIONS.

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Aims: Efficacy trials for contingency management (CM) most often utilize monetary vouchers, prizes, or clinic privileges as reinforcers. Despite sizable efficacy literature, little attention has been given to the relative efficacy of these CM applications. Consequently, the primary aim of this review is to examine comparative efficacy of published trials testing vouchers, prizes, or privileges as exclusive means of behavioral reinforcement for substance abstinence.
Methods: In total, 87 identified trials met the following criteria: 1) use of an RCT design, 2) description of setting, duration of treatment, and nature of reinforcement, 3) inclusion of substance use as an outcome, and 4) provision of data-based information to calculate Cohen's d. An effect size was then calculated for each trial, and interpreted according to established criteria (d <.50 = small, .50 < d < .80 = medium, d >.80 = large).
Results: Voucher-based reinforcement was most commonly evaluated, represented in 57 trials. Of these, 32 trial effects (56%) were small, 15 (26%) were medium, 9 (16%) were large, and 1 (2%) negative. Prize-based reinforcement was tested in 14 trials, for which 10 trial effects (71%) were small, 3 (22%) were medium, and 1 (7%) was large. Privilege-based reinforcement was tested in 16 trials, for which 11 trial effects (68%) were small, 3 (19%) were medium, and 2 (13%) were large. Thus, effect size distributions for sets of trials testing voucher-, prize-, and privilege-based reinforcement were comparable. Potential influence of other trial features (e.g., chronology, setting, sample size, CM duration, outcome variable) as predictors of effect magnitude is also explored.
Conclusions: Collective findings underscore the importance of core operant conditioning principles that bind all CM applications.
Financial Support: This review is supported by K23 DA025678 (Hartzler, PI).

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CULTURALLY TAILORING THE REAL MEN ARE SAFE HIV PREVENTION INTERVENTION.

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Aims: In the NIDA Clinical Trials Network Real Men Are Safe (REMAS) protocol (CTN0018), we found that REMAS was effective at reducing the number of unprotected sexual occasions for men in substance abuse treatment compared to a HIV education control intervention. Subsequent analysis indicated the intervention was less effective with non-white compared to white participants
Methods: Utilizing a modified Delphi Process, modules from REMAS were compared to similar content modules from culturally tailored HIV prevention interventions that were not targeted specifically to men in substance abuse treatment. Utilizing ratings and recommendations obtained from an independent expert panel REMAS was then subsequently revised to be more culturally tailored for a ethnically diverse group of men including African American and Hispanic men.
Results: Ratings suggested REMAS was culturally fair, but that in certain areas such as relationship and sexual norms, and communication skills, the culturally tailored interventions were more culturally in tune with African American and Hispanic populations. Revisions to REMAS included: 1) an added focus on how culture, social norms and upbringing affects our sexual behavior and relationships; 2) clients are engaged in more activities within the group / more doing- less watching; 3) more input from clients is generated. In a second phase of the study, currently under way, the revised intervention is being pilot tested in 4 community treatment programs with either high concentrations of African Americans or Hispanic men.
Conclusions: The Delphi Process was successfully utilized to revise the REMAS to make it more sensitive to culturally diverse populations of African American, white and Hispanic men in substance abuse treatment.
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INDIVIDUAL AND NETWORK DETERMINANTS OF BUPRENORPHINE MISUSE AMONG RURAL PRESCRIPTION OPIOID USERS.

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Aims: Despite reports of buprenorphine (BUP) misuse and diversion in the United States, little is known about risk factors for this behavior. The study purpose was to determine independent predictors of BUP misuse "to get high" among a longitudinal cohort of Appalachian prescription opioid abusers.
Methods: A total of 403 subjects are included in the analysis. Misuse was coded positive if subjects endorsed using BUP "to get high" between the baseline and 6-month interviews. Individual- and network-level factors were considered for inclusion in a multilevel random effects logistic regression model to determine risk factors.
Results: A total of 188 participants (46.6%) reported BUP misuse over the 6-months between the baseline and follow-up and 102 (25.3%) participants misused BUP in the 30 days prior to the follow-up interview. The median number of days using BUP in the past 30 was 1, indicating sporadic use, especially compared to other opioids such OxyContin, other oxycodone and hydrocodone. Individual-level predictors included baseline OxyContin use "to get high" (aOR: 1.95, 95% CI: 1.24 – 3.04) and Generalized Anxiety Disorder (aOR: 1.78, 95% CI: 1.14 – 2.78). Baseline benzodiazepine misuse "to get high" decreased risk (aOR: 0.50, 95% CI: 0.29 – 0.87). In models adjusting for individual-level characteristics and allowing network characteristics to vary across subject, having a larger drug network at baseline increased risk (aOR: 1.05, 95% CI: 1.00 – 1.10). Demographics (e.g., age, sex, race) and treatment history were not risk factors.
Conclusions: These results indicate that buprenorphine misuse "to get high" is not solely based on individual characteristics, but also social network characteristics. Thus, prevention and treatment engagement efforts may need to be more broadly focused.
Financial Support: This research is supported by NIH R01DA024598.

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HIV RISK REDUCTION COUNSELOR TRAINING FOR A RANDOMIZED CLINICAL TRIAL.

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Aims: In 2010, the National Institute on Drug Abuse Clinical Trials Network completed a study designed to evaluate strategies for providing rapid HIV testing in substance use treatment programs. Counselors from 12 sites across the U.S. were trained to provide on-site rapid HIV testing and a manualized HIV risk reduction counseling based on the RESPECT-2 model (CDC 2010).
Methods: The training team was responsible for three aspects of the intervention: counselor training, fidelity monitoring and ongoing counseling supervision. Counselor training occurred in three phases: pre-national training (conference calls to review general HIV information, rapid HIV testing, and intervention material), national training (in person, hands-on didactic and experiential practice of the intervention with immediate feedback), and post-national training (ongoing weekly group consultation calls and, if needed, individual consultation via email or telephone, to discuss actual HIV risk reduction counseling sessions during the ongoing trial). With participant consent, counseling interactions were audio-taped, and 10% were randomly reviewed by trained fidelity raters to ensure fidelity. To strengthen counselor skills by reinforcing proper techniques and sharing constructive input, the training/ supervision team provided real time written feedback to counselors on randomly reviewed session. Raters assessed required activities, using a 4-point scale. Audiotapes that averaged above 1.5 were categorized as good and those over 2.5 as excellent.
Results: Of 198 of audiotapes reviewed, 188 (94.9%) were rated excellent and the remaining 10 (5.1%), good. A subset of 35 audiotapes was reviewed by multiple raters and inter-rater agreement was 97.1%.
Conclusions: Through an intensive training implementing a variety of training modalities substance use counselors with no prior training or experience in HIV risk reduction counseling successfully conducted rapid HIV testing and HIV risk reduction counseling with substance use treatment clients.
Financial Support: Funding provided by NIDA Clinical Trials Network.

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D2 RECEPTOR PARTIAL AGONISTS: DEFINING THE ASSOCIATION BETWEEN INTRINSIC EFFICACY AND REINFORCING PROPERTIES IN MONKEYS.

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Aims: It has been reported that dopamine receptor full agonists and some, but not all, partial agonists can function as positive reinforcers in monkeys (Woolverton et al, 1984; Ranaldi et al, 2001). We have now tested the high efficacy D2 receptor partial agonist, ropinirole, in monkeys trained to self administer cocaine on a fixed-ratio (FR) schedule in an attempt to define the link between intrinsic agonist efficacy and the ability to serve as a positive reinforcer.
Methods: Male rhesus monkeys were trained to lever press to receive cocaine (0.03 or 0.1 mg/kg/inj, iv) under a FR 25 schedule. When baseline responding was stable, cocaine (0.01 to 0.3mg/kg/inj, iv), saline and ropinirole (0.0003 to 0.03 mg/kg/inj, iv) were assessed with doses available for several consecutive sessions.
Results: Both drugs maintained responding above saline levels on the FR schedule (n=4 5). As the FR response requirement was increased, cocaine was self administered at FR ratios ≤100 (1 monkey), 200 (2 monkeys) and ≤400 (2 monkeys). Ropinirole maintained self-administration at levels above saline at FR ratios ≤25 (1 monkey) and ≤100 (3 monkeys).
Conclusions: Ropinirole, which has between 64-100% intrinsic efficacy as a D2 receptor agonist (Gardner and Strange, 1998; Al Fulaij et al, 2007; Coldwell et al, 1999), functioned as a positive reinforcer on a FR 25 schedule of reinforcement, but responding at higher response requirements demonstrated that it was substantially less reinforcing than cocaine. In terms of intrinsic D2 agonist efficacy (see previous references & Lahti et al, 1992), it has been shown that bromocriptine (58-100%) and piribedil (77%) can serve as positive reinforcers, whereas terguride (16%) and S(-) 3 PPP (10 34%) do not (Woolverton et al, 1984; Ranaldi et al, 2001). Our results with ropinirole add to this database and confirm that >50% intrinsic efficacy is required for D2 partial agonists to have the potential for positive reinforcing effects in monkeys.
Financial Support: Abbott Healthcare Products BV

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INFANT PUPIL DIAMETER IN RESPONSE TO OPIOID ADMINISTRATION.

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Aims: Pupil diameter is a frequently assessed objective index of the pharmacodynamic effects of opioids in humans. For example, opioid administration in adults results in pupil constriction, followed by progressive dilation as the drug is metabolized. The pupillary effects of opioids are easily measured photographically in adults, but to our knowledge, have never been measured in infants. Extension of this objective, sensitive measure of opioid effects could aid in the more accurate assessment and treatment of neonatal abstinence syndrome (NAS) in infants exposed to opioids prenatally. As an initial step towards this overarching aim and as proof of concept, the present study examined changes in pupil diameter in response to opioid administration in opioid-exposed infants who required pharmacological treatment for NAS.
Methods: Participants were 8 infants (2-7 days old) who were stabilized on methadone (0.4-0.5 mg/kg q12h). Pictures of one of each infant's eyes were taken under controlled illumination conditions (20-40 lux) with a standard digital camera just prior to dosing and approximately 0.5, 3, 6, 9, and 12 hours after dosing. Picture files were transferred to a computer and ImageJ software was used to measure the diameter of the pupil and the iris. Relative pupil diameter (pupil diameter ÷ iris diameter) was calculated and analyzed.
Results: There was a significant main effect of time overall and a significant linear trend for the post-dose measurements. Prior to dosing, relative pupil diameter was 41%; post-dose, it was 29%, 33%, 38%, 41%, and 43% at 0.5, 3, 6, 9, and 12 hours post-dose, respectively. Measurements at 0.5 and 3 hours post-dose were significantly lower compared to baseline.
Conclusions: Results indicate that pupil diameter can be measured photographically in opioid-exposed infants and that infant pupils respond to opioid administration in the same manner as adults. Future studies should examine the reliability and validity of pupil diameter as a measure of NAS in opioid-exposed infants.
Financial Support: NIDA T32DA7242

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PRELIMINARY PHARMACOGENETIC STUDY OF TREATMENT FOR METHAMPHETAMINE DEPENDENCE.

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Aims: To perform an exploratory pharmacogenetic study of response to modafinil for the treatment of methamphetamine (MA) dependence.
Methods: Non-Hispanic Caucasian (N=35) and Hispanic Caucasian (N=26) MA dependent participants of a randomized, double-blind, placebo controlled trial of modafinil, with cognitive behavioral therapy and contingency management, for MA dependence were genotyped for three single nucleotide polymorphisms previously found to influence cognition and amphetamine response: COMT Val158Met, BDNF Val66Met, and OPRM1 Asn40Asp. Treatment outcomes (MA use and retention) were compared by genotype within each ethnicity.
Results: BDNF Val66Met was significantly associated with MA use during treatment (p=0.039), but not retention, after controlling for age, gender, baseline MA use, and treatment group (modafinil versus placebo) among non-Hispanic Caucasian but not Hispanic participants. There were no significant main effects for COMT Val158Met and OPRM1 Asn40Asp on treatment outcomes in either ethnic group, but there was a significant medication by COMT Val158Met interaction with lower MA use on modafinil relative to placebo among Hispanics with Val/Val genotype.
Conclusions: Results are preliminary and require confirmation in prospective, adequately powered samples but may provide guidance in the design of pharmacogenetic studies of medications for MA dependence.
Financial Support: NIDA Grants 1 K23 DA 023558 (Heinzerling) and 1 P50 DA 18185 (Shoptaw). Study medication and matching placebo was provided by Cephalon, Inc.

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GABRA2 GENOTYPE INFLUENCES RISK FOR SUBSTANCE ABUSE VIA EFFECTS IN THE NUCLEUS ACCUMBENS.

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Aims: Substance abuse and related externalizing disorders have been associated with variants in *GABRA2*, a gene encoding the $GABA_A^{\alpha 2}$ receptor subunit. Recently, parenting was found to moderate the relationship between *GABRA2* and externalizing problems, a risk factor for addiction. However, the neural mechanism through which *GABRA2* influences risk remains largely unstudied. Drugs of abuse exert their reinforcing properties by activating the mesolimbic dopamine circuitry, which originates in the ventral tegmental area and projects to the nucleus accumbens. This pathway is regulated by GABAergic interneurons. We tested the hypothesis that *GABRA2* genetic variation is linked to individual differences in nucleus accumbens response to salient stimuli, and that these differences relate to risk for substance abuse.
Methods: We studied 18-21 year olds (n=45) using functional MRI during a monetary incentive delay task. Sample size for each genotype (SNP rs279858) was: 11 A/A, 24 A/G, 10 G/G. Parenting was determined from a 26 item composite index which covers parents' attitudes about adolescent drinking, their own drinking and drug use, time spent with their children and parental monitoring as reported by both the child and the parent when the child was 12–14 years old.
Results: We found that *GABRA2* genotype was associated with varying levels of nucleus accumbens activation to incentive anticipation, and that parenting moderated this effect. Furthermore, nucleus accumbens activation was associated with levels of drinking and drug use, an effect that was also moderated by parenting. Tests of indirect effects revealed that nucleus accumbens activation significantly mediated the relationship between *GABRA2* genotype and levels of drinking and drug use in those who experienced worse parenting.
Conclusions: This work uncovers a neural pathway through which *GABRA2* genotype may influence risk for addiction and highlights an important environmental factor that moderates this risk.
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THE RELATIONSHIP BETWEEN GENDER AND EXPECTANCIES FOR THE PROCESS OF SMOKING CESSATION.

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Aims: Women appear to be less likely to attempt to quit smoking and less likely to successfully cease cigarette use as compared to men. The aim of the present investigation was to explore a set of potential underlying factors driving this gender difference: the expectancies that smokers hold about the process of smoking cessation, i.e. abstinence-related expectancies.
Methods: 501 smokers (231 women, 270 men) completed the Smoking Abstinence Questionnaire (SAQ; Hendricks et al., in press), a new measure that assesses smokers' abstinence-related expectancies on 10 scales: Withdrawal, Social Improvement/Nonsmoker Identity, Adverse Outcomes, Treatment Effectiveness, Common Reasons, Barriers to Treatment, Social Support, Optimistic Outcomes, Coffee Use, and Weight Gain. Participants also completed a number of questionnaires assessing demographic characteristics and smoking-related variables.
Results: A multivariate analysis of variance revealed significant differences between men and women across the 10 scales of the SAQ ($\Lambda = .94$, $p = .0007$). Post-hoc analyses revealed that women reported stronger expectancies for Withdrawal ($F = 4.5$, $p = .03$), Barriers to Treatment ($F = 6.0$, $p = .015$), and Weight Gain ($F = 8.0$, $p = .005$), and weaker expectancies for Social Improvement/Nonsmoker Identity ($F = 3.7$, $p = .055$). Additional analyses indicated that a number of demographic and smoking-related variables may mediate the relationship between gender and abstinence-related expectancies.
Conclusions: Findings suggest that smoking cessation may represent a more daunting prospect for women because they anticipate more aversive withdrawal symptoms, greater difficulty obtaining pharmacotherapeutic and professional intervention, more weight gain, and less improvement in their social functioning when they quit smoking. These results may prove useful in directing more efficacious smoking interventions for women.
Financial Support: This study was supported by the NIDA grant F32 DA024482 as well as the State of California Tobacco-Related Disease Research Program grant 16FT-0049.

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TOBACCO PRODUCT DEPENDENCE LIABILITY ASSESSMENT TO SUPPORT THE WHO FRAMEWORK CONVENTION ON TOBACCO CONTROL.

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Aims: Describe the global public health need for guidance for reducing the dependence liability and attractiveness of tobacco products, and the potential implications for scientists involved in abuse liability assessment research.
Conclusions: The WHO FCTC came into force in 2005 with 172 parties by 2010. The FCTC and emerging tobacco regulation in many nations (e.g., by Health Canada and the FDA) require attention to the dependence liability and attractiveness of tobacco products. The 2010 Conference of Parties guiding FCTC implementation concluded that tobacco product addictiveness and attractiveness must be controlled to reduce tobacco use, disease, and death. In response, the WHO Tobacco Regulation Study Group (TobReg) developed a report on a framework for regulation of tobacco product dependence liability. It discusses the importance of tobacco product designs, contents, and emissions in their use, dependence liability, attractiveness, and harmfulness. The conclusions and recommendations will be presented at CPDD. These include the following: (1) A regulatory framework for reducing dependence potential is vital. (2) Regulatory actions to reduce dependence should also consider actions to reduce product attractiveness because these can also contribute to initiation and the development of dependence. (3) Regulation of nicotine content and delivery should be guided by predicted impact on public health. (5) Regulatory actions addressing dependence liability, product attractiveness, and nicotine should be accompanied by surveillance to detect the consequences in a timely manner. (6) Several areas of research will be vital to advance the science foundation for this area of tobacco product regulation.
Financial Support: WHO TobReg work on the report was supported by WHO. Pinney Associates supports JEH's efforts to develop this abstract, the poster and travel to CPDD.

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TRAUMA EXPOSURE, DISTRESS, AND MEASURES OF IMPULSIVITY IN COCAINE DEPENDENCE.

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Aims: Both impulsivity and traumatic experiences are risk factors for substance use and dependence. There may be an association between impulsive behaviors, history of traumatic life events and/or posttraumatic stress disorder (PTSD) symptoms, and this study evaluates whether a history of trauma exposure is significantly associated with current impulsive behavior/decision making among participants enrolled in an ongoing clinical trial of cocaine dependence treatment during methadone maintenance.
Methods: Participants (N=74, AA:62%, F:51%, age: 42±7) completed cognitive assessments during a methadone run-up phase and were evaluated for a history of trauma exposure and measures of impulsivity and decision-making. Correlational analyses were conducted between trauma-related questionnaires (Traumatic Life Events Questionnaire (TLEQ) and PTSD Symptom Scale (PSS)) and measures of impulsivity (Barrett Impulsiveness Scale (BIS-11) and Zuckermann-Kuhlmans's Personality Questionnaire (ZKPQ)) and decision-making (Iowa Gambling Task (IGT) and Delay Discounting). Comparisons were then made between participants reporting PTSD symptoms ≤8 (PSS (-), N=53) and >8 (PSS (+), N=17). Correlations were also conducted between severity of PTSD symptoms and measures of impulsivity/decision-making within the PSS (+) group.
Results: There were no differences in demographics or past drug use history between PSS (+) and PSS (-) groups. PSS (+) scored higher in the cognitive impulsivity factor (U=308.5, p=0.05) of the BIS. Within the PSS (+) group, there was no significant correlation between number of symptoms endorsed and impulsivity measures. Total number of traumatic events reported correlated with the impulsive/sensation seeking (r=0.26, p=0.04) and activity (r=0.32, p=0.01) traits of the ZKPQ. Neither TLEQ nor PSS scores correlated with IGT or rates of discounting.
Conclusions: Some aspects of impulsivity may be associated with of a history of traumatic life events. These findings demonstrate a potential relationship between traumatic events and subsequent impulsivity.
Financial Support: Supported by DA021808 and DA023186.

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COGNITIVE FUNCTIONING, MENTAL HEALTH AND SUBSTANCE USE SEVERITY IN ADULTS WITH A HISTORY OF METHAMPHETAMINE USE.

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Aims: This study describes cognitive functioning and its relation to psychiatric and substance use severity among adults with long duration methamphetamine (meth) use careers.
Methods: Data are from a 2009-10 long-term follow-up interview in an intensive natural history study of adults (N=253) who had used meth regularly at recruitment in 1999-2003. Subjects initiated use an average of 23 years prior to the interview; 24% used in the 30 days prior to the follow-up interview. Subjects completed the Automated Neuropsychological Assessment Metrics (ANAM), including the Code Substitution Delayed (CDD) test of delayed recall. CDD accuracy, speed and efficiency (i.e., correct responses/minute) scores were examined in relation to demographic, mental health and substance use measures. Depression was assessed using the Beck Depression Inventory.
Results: The mean CDD scores were: accuracy=74.5 (SD=16.1), speed=31.8 (SD=11.3) and efficiency=23.4 (SD=10.5). Correlations (significant at $p<.05$) revealed that: more education was associated with higher accuracy; older age was correlated with lower speed and efficiency; and more days of recent meth use was related to higher speed and lower accuracy. Younger age at first meth use was related to lower speed and efficiency. Higher depressive symptomatology was related to lower accuracy and efficiency. Participants with at least 1 year of meth abstinence had higher accuracy scores than those who used meth in the past year ($p<.05$). Regular use of crack cocaine ($p<.05$) and regular use of tranquilizers ($p<.05$) were also related to lower accuracy. Multivariate analyses further examine the relationship of cognitive functioning and patterns of substance use severity and mental health, adjusting for age and education.
Conclusions: While previous research has linked meth use with significant cognitive impairment, these findings suggest that early initiation, recent substance use and recent mental health problems are related to cognitive deficits in aging adults with long meth use careers.
Financial Support: NIDA DA025113

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SUBSTANCE ABUSE PROBLEMS AMONG MINORITY TEENS PRESENTING TO A GENERAL OUTPATIENT PSYCHIATRY CLINIC.

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Aims: Research has shown that adolescent boys are more likely to have substance abuse problems than girls. However, little research has examined gender and racial differences in substance use problems in a minority population seeking outpatient mental health treatment.
Methods: From a sample of 64 urban minority youth, 52 identified as Hispanic (61.5%) and African American (38.5%). Of these 52, 57.7% were female with a mean age of 14.92 (1.4) years. Participants recruited in the waiting room completed the Personal Experience Inventory (PEI) to examine risk factors for substance use; demographic and diagnostic information was extracted from the medical record. Chi Square tests and ANOVA were used to compare gender and race on demographics and diagnosis and MANOVA on PEI scale scores, while controlling for days in treatment.
Results: A main effect was found for gender ($F(1,26) = 1.9$, $P = .04$); no race or interaction effects emerged. Contrary to expectations, girls trended towards higher rates of substance use disorders ($X2(1) = 3.1$, $p=.07$) and also evidenced greater risk on the PEI ($F(1, 28) = 2.0$, $p=.04$) than boys. Girls endorsed more poly drug use ($p=.01$), psychological benefits of drug use ($p=.02$), transsituational drug use ($p=.05$), rejecting convention ($p=.00$), family pathology ($p=.05$), and absence of goals ($p=.04$). In addition, trends were found for girls to have greater personal involvement with drugs ($p = .06$) and to experience more consequences due to drug use ($p=.06$).
Conclusions: Unlike prior studies, in our minority sample of adolescents in outpatient mental health treatment, girls were more likely to be substance involved and to have more substance use risk factors than boys. Teens entering psychiatric treatment should be screened for addiction problems and stereotypes of boys having more substance abuse problems should be re-thought among minority samples in a general clinic setting.
Financial Support: Child and Family Institute, St. Luke's - Roosevelt Hospital.

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IMPROVING HIV/AIDS KNOWLEDGE AMONG COCAINE-DEPENDENT OUTPATIENTS.

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Aims: One third of all new cases of HIV/AIDS in the U.S. are drug use related. Knowledge of HIV transmission is an important determinant of HIV-related risk behavior, making development of interventions to increase HIV knowledge among high-risk populations such as substance abusers is an important first-line prevention strategy. However, only about 50% of outpatient substance abuse treatment programs provide HIV/AIDS education, likely due to the cost and complexity of existing evidence-based interventions. Our primary aim is to evaluate the efficacy of a brief HIV/AIDS educational intervention.
Methods: Cocaine-dependent outpatients (N=53) completed HIV/AIDS knowledge tests at study intake to assess baseline knowledge. Patients were then randomly assigned to an HIV/AIDS educational intervention (experimental condition; n=29) or a sham intervention (control condition; n=24). The educational intervention consisted of the patient meeting with a therapist to view an HIV/AIDS education video, review an HIV/AIDS education pamphlet, and review their pretests, with emphasis placed on providing corrective feedback on items answered incorrectly or "don't know." Patients then completed the knowledge tests a second time.
Results: Scores on tests increased significantly from baseline (17%, $p < .001$) among patients who completed the educational intervention, but not among patients who completed the sham intervention (1%, $p > .05$). Control condition patients were subsequently crossed over to receive the educational intervention, and test scores increased significantly from baseline (19%, $p < .001$). Patients in both conditions (n=37) completed follow-up tests approximately 6 weeks after completing the educational intervention. Scores on follow-up tests were significantly higher than baseline scores in both conditions (13%, $p < .05$).
Conclusions: These results support this inexpensive and easily implemented intervention's efficacy for increasing HIV/AIDS knowledge among cocaine-dependent outpatients. It would likely be equally as effective in other populations.
Financial Support: R01DA009378 & T32DA07242

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PRE-CONCEPTION MARKERS OF DUAL RISK FOR ALCOHOL AND SMOKING EXPOSED PREGNANCY: TOOLS FOR PRIMARY PREVENTION.

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Aims: Effective pre-conception primary prevention strategies are needed for women who are dually at risk for alcohol- and smoking-exposed pregnancies. Women who continue to smoke and/or drink during pregnancy are typically intractable to change, but there are evidence-based methods to help women change before conception, maximizing the chances of a healthier pregnancy. This study sought to identify risk factors that can be used to identify and intervene with women in need of pre-conception intervention.
Methods: Over 2 years, 217 women, 109 at risk for alcohol exposed pregnancy (AEP) and smoking exposed pregnancy (SEP) and 108 women at risk for AEP only were recruited from central Virginia. All participants completed a battery of instruments including assessments of sexual, smoking, drug use, and alcohol history and current behavior on the TLFB, MINI, TWEAK, WHO ASSIST, and AUDIT-C. Women at dual risk for SEP/AEP were compared to women at risk for AEP using t-tests and Chi-square analyses.
Results: Several factors differentiated dual from single risk women, including lower education and employment, higher sexual frequency and non-marital cohabitation, less use of contraception, and higher frequency of alcohol use and other mental disorders among dual risk women. Dual risk women had earlier onset of intercourse and contraception, and higher rates of STI testing and number of live births. Dual risk women had higher rates of ineffective or no contraceptive methods. Dual risk women smoked daily with 9 CPD; 80% were nicotine dependent, smoking within 30 minutes of waking. Dual risk women drank 4 or more days per week, and had higher rates of heavy drinking and use of marijuana.
Conclusions: Women at dual risk for SEP/AEP are a more severe group who may be more likely to have unintended pregnancies. The importance of pre-conception prevention efforts for this group is clear. Several measurable factors differentiate SEP/AEP women and these factors could be used to target primary prevention efforts efficiently.
Financial Support: R01AA14356

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RISK OF DEATH DURING AND AFTER OPIATE SUBSTITUTION THERAPY IN PRIMARY CARE.

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Aims: Does the effect of opiate substitution treatment (OST) on drug related mortality vary at the beginning and end of treatment and according to treatment duration?
Methods: Primary care patients on the UK General Practice Research Database prescribed methadone or buprenorphine during 1990-2005, involving 5,577 patients followed-up (17,732 years) until death or one year after the expiry of their last OST prescription. Treatment was the main exposure and mortality was the main outcome. 178 (3%) patients died during follow-up; 62 on treatment.
Results: Crude mortality rates (CMR) were 0.7 per 100 person years (p100py) on OST and 1.3 p100py off treatment: 5.3 and 10.9times higher than general population. The mortality rate was almost twice as high among men compared to women. In the first two weeks of OST the CMR was 1.7p100py: 3 times higher (after adjustment for sex, age-group, calendar period and comorbidity) than the mortality rate during the rest of time on treatment (CMR 0.7p100py). The CMR was over 4.0p100py in weeks 1-4 after treatment and 0.95 p100py during the rest of time off treatment: over 8 and nearly 2 times higher than the baseline risk of mortality during treatment. The death rate in the first month after treatment was over 4 times higher than in the subsequent period off treatment . We estimate that average treatment durations of <30 weeks have a low probability (<25% chance) of reducing the overall risk of death; but at treatment durations approaching or greater than a year there is >85% chance that OST will reduce the risk of overall mortality in opiate users.
Conclusions: Clinicians and patients should be aware of the increased mortality risk at the start of opiate substitution treatment and immediately after stopping treatment. The relationship between average duration of treatment and overall drug related mortality needs further investigation; and may explain why in the UK increases in OST may have not led to an observed decrease in the number of drug related deaths.
Financial Support: UK NIHR CRDHB MRC New Investigator Award

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TOBACCO USE CHARACTERISTICS AND QUIT ATTEMPTS AMONG SMOKERS WITH SERIOUS MENTAL ILLNESS.

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Aims: To examine readiness to quit, thoughts about abstinence and psychiatric symptoms among smokers with serious mental illness.
Methods: Participants (N=100) were recruited from smoke-free psychiatric units in 2009-10 at a large, urban, county hospital and reported demographic, tobacco, and clinical characteristics.
Results: The sample smoked a mean (SD) of 20 cigarettes/day (12); smoked for 23 years (13); 80% smoked within 30 min of awakening; 53% smoked menthols; 44% attempted to quit in the past year; and 74% quit cold turkey in past quit attempts. Stage of change for quitting smoking was 33% precontemplation, 42% contemplation and 25% preparation. Ratings of perceived difficulty with quitting were higher (M=6.9, SD=3.1) than ratings of desire to quit (M=5.9, SD=3.2) and anticipated success (M=5.7, SD=2.9). Smoking goals were 28% no goal, 47% restricting current smoking and 25% quit for good. In the past year, 43% were advised to quit smoking by a mental health provider. Diagnoses were 54% unipolar and 14% bipolar depression and 46% psychotic disorder; 75% had a prior psychiatric hospitalization. The sample had clinically significant depressive symptoms (mean CESD=16, SD=8.1), which positively correlated with smoking within 30 min of awakening (r=.23, p=.02) and perceived difficulty maintaining abstinence (r=.27, p=.008), but also stronger desire to quit (r=.29, p=.004). Heavier smokers perceived greater difficulty with maintaining abstinence (r=.27, p=.008) and less success with quitting (r=-.30, p=.002). Past-month substance use included alcohol (67%), marijuana (49%), cocaine (42%) and methamphetamine (32%). Substance abuse (r=.29) and psychotic symptoms (r=.28) were associated with greater desire to quit smoking (p's<.01).
Conclusions: In this diverse sample of smokers with serious mental illness, a sizable proportion do want to quit tobacco but anticipate difficulty and are not well supported in quit attempts. The need for treatments will be discussed.
Financial Support: This research was supported by grants K23DA018691, P50DA09253 and T32DA007250.

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COGNITIVE BEHAVIORAL THERAPY AND THE NICOTINE TRANSDERMAL PATCH FOR DUAL NICOTINE AND CANNABIS DEPENDENCE: A PILOT STUDY.

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Aims: The prevalence of nicotine and cannabis dependence is high and poses significant public health problems. There are currently no integrated treatments that address this dual dependence. We assessed the feasibility of using a combined cognitive behavioral therapy (CBT) plus transdermal patch nicotine replacement therapy (NRT) to treat co-occurring nicotine and cannabis dependence.
Methods: A total of 11 adults (7 female and 4 male), with a DSM-IV diagnosis of both nicotine and cannabis dependence, consented to 10 weekly 50-minute CBT sessions while wearing a transdermal nicotine patch for 10 weeks. Our manual was based upon the Marijuana Treatment Protocol (Steinberg et al 2005), with elements of Munoz et al's (1988) CBT for smoking cessation. The CBT was aimed at changing marijuana and tobacco cigarette use through skill building and monitoring thoughts, daily activities, interpersonal contacts, and mood. Cigarette use, urinary cotinine, cannabis use, THC-creatinine ratio, and scores on the Client Satisfaction Questionnaire (CSQ-8) were determined at baseline, 4, 6, 8, and 10 weeks. Data were analyzed using repeated-measures ANOVA.
Results: Eight individuals completed the 10-week trial (72.2%). Subjects smoked 12.7 ± 5.6 tobacco cigarettes/day at baseline, which was reduced to 2.73 cigarettes/day at the end of treatment ($F(5) = 18.4$, $p<.001$). Subjects also reduced their marijuana from 9.20 ± 5.29 hits at baseline to 7.25 ± 5.62 hits at 10 weeks ($F(4) = 1.77$, $p=.17$). Mean CSQ-8 scores were uniformly high over the 10 weeks of the study (30.6 ± 1.88).
Conclusions: A 10-week combined CBT plus NRT treatment program significantly reduces tobacco use and marginally reduces marijuana smoking in a group of dually dependent tobacco and marijuana users. Adding more emphasis on marijuana use in the CBT program or a pharmacological component may increase efficacy of this dual approach.
Financial Support: Norman E. Zinberg Fellowship in Addiction Psychiatry Research, Harvard Medical School

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12-STEP GROUP PARTICIPATION IN OPIOID-DEPENDENT PATIENTS RECEIVING BUPRENORPHINE AND BEHAVIORAL TREATMENTS.

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Aims: The effectiveness of 12-Step programs for initiating and maintaining abstinence has been documented for opioid dependent individuals, although some reports describe 12-Step programs as not accepting attendees who are receiving opioid substitution therapy. No research, however, has examined the relationship between combined buprenorphine pharmacotherapy and behavioral interventions and 12-step program participation.
Methods: The current analyses address 12-Step group participation in 122 opioid-dependent adults participating in an ongoing NIDA-sponsored study of pharmacotherapy and randomized behavioral treatment. In addition to treatment with buprenorphine/naloxone (Suboxone) and medication management, participants were randomly assigned to a 16-week behavioral treatment condition (Cognitive Behavioral Therapy, Contingency Management, Both CBT+ CM, Neither CBT nor CM). Self-help assessments were completed at baseline and after the behavioral treatment phase.
Results: The percentage of study participants who reported having attended 12-Step groups in the previous 6 months increased significantly from baseline (60.4%) to week 16 (77.78%; $p < 0.000$). Other significant changes from baseline to Week 16 include an increase in the percentage of participants who reported having a sponsor (17.0% to 30.9%; $p = 0.002$). Additional analyses, such as the association between 12-Step group participation and opioid use, and comparisons of the subgroups based on 12-Step group participation are also presented and discussed.
Conclusions: The association between 12-Step group participation and drug use has clinical implications: Pharmacological and behavioral treatment providers should routinely emphasize the benefits of 12-Step group participation to their patients.
Financial Support: The National Institute on Drug Abuse (R01 DA 020210)

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SUBSTANCE-DEPENDENT, CONDUCT-DISORDERED ADOLESCENTS: SEVERITY OF DIAGNOSIS DOES NOT PREDICT FUTURE INCARCERATION RISK.

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Aims: Background: Adolescent substance use disorder (SUD) is often co-morbid and worsened by conduct disorder (CD). CD and SUD have been both described as predictors of criminal behavior and incarceration, but it is unclear that the diagnostic severity of these conditions predicts future incarceration risk.
Methods: Methods: This prospective study tests the hypothesis that CD and SUD severity of diagnosis, defined by number of symptoms endorsed at baseline, predicts future incarceration, assessed at 2nd interview. Substance-dependent and conduct-disordered adolescents (N=520), enrolled in a family study of CD and SUD, were first interviewed between 1993 and 2006 (ages 13-19), and then again, between 2004 and 2010 (ages 18-33). We examined SUD, CD and incarceration status in both occasions.
Results: Results: Neither diagnostic severity of CD nor of SUD was associated with future incarceration risk. Being previously arrested (before study enrollment) (chi-square; $df=1$; $p<0.0001$), and younger age at study enrollment (t test; $df=518$; $p=0.0283$) were associated with higher risk of future incarceration.
Conclusions: Conclusions: Contrary to our hypothesis, CD and SUD diagnostic severity did not predict future incarceration risk. Results support that earlier involvement in the juvenile system alone does predict such risk.
Financial Support: Supported by P60DA011015, R01DA012845, R01DA021913.

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ADOPTION OF A RAPID HIV TESTING AND COUNSELING PROGRAM FACILITATES STATE-WIDE IMPLEMENTATION.

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Aims: To report on an initiative to implement HIV rapid testing in substance abuse treatment programs in the state of South Carolina. A multi-agency collaboration between the Single State Authority, the state Health Department, the regional Addiction Technology Transfer Center, and one substance abuse treatment program that adopted a rapid HIV testing and counseling program following the completion of a clinical trial, facilitated state-wide implementation. LRADAC,a community-based treatment program, was one of twelve sites that participated in a randomized clinical trial,sponsored by the NIDA/CTN,(CTN0032)HIV Rapid Testing and Counseling in Drug Abuse Treatment Programs. Upon completion of the trial, LRADAC implemented a rapid HIV testing and counseling program as a clinical service. South Carolina's previous efforts to implement on-site rapid HIV testing in 10 pilot agencies had less than optimal success due to the absence of a successful model on which agencies could base their implementation plan. With support from the collaborating agencies, staff developed and presented a 2 ½ day HIV testing and counseling curriculum at the annual SC School of Alcohol and Drug Studies in 2010.Following the successful completion of the course, participants were fully certified to conduct testing and counseling in their local programs. Course participants had the opportunity to learn the counseling and testing procedures that LRADAC staff found successful in implementing their program.
Conclusions: Although challenging, implementing HIV testing programs in substance abuse treatment programs is feasible for agencies. The multi-agency collaboration in South Carolina supported the development of an HIV testing and counseling course that was team taught and showcased a successful model on which implementation could be based.Consequently, this effort increased the likelihood that additional substance abuse agencies within the state would move forward with implementation.
Financial Support: Multi-agency collaboration.

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REINSTATEMENT OF METHAMPHETAMINE SEEKING IN MALE AND FEMALE RATS TREATED WITH MODAFINIL AND ALLOPREGNANOLONE.

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Aims: Sex differences in methamphetamine (METH) use have been demonstrated in clinical and preclinical studies. The aim of this experiment was to investigate the effect of sex on the reinstatement of METH-seeking behavior in rats. Another aim was to determine if there were sex differences in pharmacological interventions for relapse; specifically, modafinil (MOD), an analeptic, and the neuroactive steroid and progesterone metabolite, allopregnanolone (ALLO).
Methods: Male and female rats were trained to self-administer i.v. infusions of METH (0.05 mg/kg/infusion). Next, rats self-administered METH for a 10-day maintenance period. Following maintenance, METH was replaced with saline and rats extinguished lever-pressing behavior for 18 days. Rats then began a multi-component reinstatement procedure in which they received priming injections of METH (1 mg/kg) at the start of each daily session, preceded one-half hour by either a treatment or control injection. Treatments consisted of MOD (128 mg/kg, i.p.) or ALLO (15 mg/kg, s.c.), and each treatment or control condition was separated by a day in which rats received only saline priming injections. MOD or control were also administered as priming injections at the onset of session to determine if MOD would induce reinstatement of METH-seeking.
Results: Female rats showed greater METH-induced reinstatement responding compared to male rats following control treatment injections. MOD significantly attenuated METH-seeking behavior in both male and female rats compared to controls; however, ALLO reduced METH-seeking only in females. MOD alone did not induce the reinstatement of METH-seeking behavior.
Conclusions: These results support the growing literature that suggests females to be more susceptible to stimulant abuse compared to males. Further, they illustrate the promise of MOD as a possible prevention for METH relapse in both males and females, but limit the scope of allopregnanolone's treatment efficacy to females.
Financial Support: DA018151S1 (TEP), R01DA003240, R01DA019942, K05DA015267 (MEC)

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THE ROLE OF CONDUCT DISORDER IN INITIATION OF SUBSTANCE USE.

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Aims: To examine the influence of Conduct Disorder (CD) on initiation of substance use
Methods: Structured interviews were administered at 2 time points to assess CD and substance use among a clinical sample of adolescents (n=249) initially recruited from a SUD treatment program and a demographically matched community sample (n=122). Ninety percent were males, 60% were white, and 78% had a CD diagnosis at time 1 or 2. Subjects were followed from adolescence (mean age=16.4, SD=1.3) into young adulthood (mean age=23.8, SD=2.8). Young adult retrospective reports of substance initiation of regular alcohol use, 5+ times cannabis use, and 5+ times cocaine use by whether subjects reported CD at either time were analyzed using Cox regression models, while controlling for age at time 1, sex, and race. These models were analyzed for the entire sample (n=371) and with the community sample only.
Results: At age 15, subjects with CD had a 3.5 times higher hazard of initiating regular alcohol use. For community subjects only, those with CD at age 15 had a 3.9-fold higher hazard of initiating regular alcohol use. At age 15, subjects with CD were 4.5 times more likely to initiate cannabis use. For community subjects only, those with CD were 2.5 times more likely to initiate cannabis use at all ages (95% CI: 1.5, 4.2). Subjects with CD at age 15 had a 33.7 times higher hazard of initiating cocaine use. For community subjects only, those with CD were 6.5 times more likely to initiate cocaine use at all ages (95% CI: 2.4, 17.4). The 4 models, for which hazard ratio at age 15 was illustrated, revealed decreasing HRs.
Conclusions: Adolescents with CD have a greater risk of initiating substances and younger median onset ages in comparison to those without CD, although this (relative) difference in risks diminishes at an older age for the models with everyone as well as for alcohol use in the community group only.
Financial Support: P60DA011015, R01DA012845, R01DA021913

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MODELING THE ASSOCIATION OF TRANSMISSIBLE RISK, SEXUAL MATURATION AND PEER AFFILIATION ON THE DEVELOPMENT OF CANNABIS USE DISORDER: A LONGITUDINAL STUDY.

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Aims: Pubertal timing, peer affiliation and transmissible liability are related to cannabis use disorder (CUD) outcome. The overarching goal of this study was to determine if pubertal timing mediates the association between transmissible risk in youth and CUD in adulthood. We hypothesized earlier sexual maturation mediates the relation between transmissible risk and CUD via affiliation with deviant peers.
Methods: Boys ascertained at age 10-12 via proband fathers with substance use disorder (SUD, N= 216) and without SUD (N= 234) were tracked through sexual maturation until age 22. Participants were evaluated at ages 10-12 and 16 using the Transmissible Liability Index to quantify intergenerational risk for SUD (Vanyuykov et al., 2009); nurse examination to document Tanner stage; and peer affiliation patterns using self-report questionnaires. Lifetime CUD was diagnosed at age 22 via structured interview. Path analysis was conducted to model the relationship among transmissible risk, pubertal timing, and deviant peer affiliation during adolescent development and CUD by age 22.
Results: Transmissible risk in childhood directly predicted CUD but was not correlated with pubertal stage. Early sexual maturation, mediated by affiliation with deviant peers, predicted CUD. Deviant peers at age 10-12 predicted transmissible risk severity at age 16.
Conclusions: These findings extend prior studies by demonstrating early pubertal timing amplifies risk for CUD, however, it does so via mechanisms unrelated to transmissible risk. Risk for CUD related to pubertal timing is mediated by contextual factors, such as affiliation with deviant peers, pointing the role of social contagion on development of psychological characteristics associated with transmissible risk for CUD.
Vanyukov, M., Kirisci, L., Moss, H., Tarter, R., et al. (2009). Measurement of the risk for substance use disorders: Phenotypic and genetic analysis of an index of common liability. Behav Genet, 39, 233-244.
Financial Support: 2K12-DA000357-11, P50-DA05605

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RELATIONSHIP BETWEEN EXECUTIVE FUNCTIONING AND INTELLIGENCE IMPLICATIONS FOR ADDICTIONS TREATMENT.

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Aims: While deficits in executive functioning have been identified in many drug abusers, intelligence is usually considered to be unimpaired. The relationship of executive functioning to intelligence needs to be clarified in clinical populations. This poster examines the relationships between two measures of intelligence and executive functioning in a clinical sample in order to clarify the relationship.
Methods: Sixteen adult patients referred for neuropsychological evaluation were administered full neuropsychological batteries that included the Reynolds Intellectual Assessment Scale (RIAS), a measure of intelligence and the Test of Verbal Conceptualization and Fluency (TVCF) a measure of executive functioning and symptom validity measures. The RIAS includes measures of verbal intelligence, nonverbal intelligence and a composite index of both verbal and nonverbal intelligence. The TVCF includes measures of verbal fluency, card sorting and trail making. The patients included 10 females, 15 Caucasians and 1 African-American, and all but one patient was right handed. Diagnoses include head trauma-6, stroke-4, brain tumor-2, anoxia-1 Multiple Sclerosis (MS)-1, Epilepsy-1 and Hydrocephalis-1. Ages ranged from 22-77 (Mean-43, Standard Deviation-14.0) and education ranged from 10-18 years (Mean-14, Standard deviation-2.2). All subjects signed inform consent documents.
Results: Correlations ranged from .64 (verbal intelligence/perseverative card sorting errors) to .16 (nonverbal intelligence/phonemic verbal fluency).
Conclusions: Correlations between intelligence and executive functioning were moderate to low as expected. Executive functioning variances were not accounted for by intelligence supporting the construct of executive functioning as a possible factor in addictions treatment.
Financial Support: Supported by private funding

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PROJECT ENGAGE: SBIRT WITH MEDICALLY HOSPITALIZED PATIENTS.

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Aims: Patients with untreated SUDs often present to hospitals for treatment of substance-related medical problems. A pilot program was conducted to identify, refer, and engage patients in community based SUD treatment to reduce subsequent hospitalizations and other costly services.
Methods: An embedded interventionist provides patients suspected of having untreated SUDs with one or more bedside assessment/MI sessions and a referral or facilitated admission to treatment. De-identified insurance claims data of a small sample of patients were reviewed over a 6-month period.
Results: Between 09/01/08 and 06/10/10, 313 patients consented to speak with the interventionist. Of them, 109 (35%) were successfully admitted to 33 community-based in/outpatient SUD programs. Insurance claims data of 18 of them over a 6-month period (3 months pre and post) showed a 33% decrease ($35,938) in inpatient medical admits, a 38% ($4,248) decrease in ER visits, a 42% ($1,579) increase in psych/SUD inpatient admissions, a 33% ($847) increase spent in psych/SUD outpatient visits, and an 88% ($1281) increase in primary care subsequent to intervention. Overall, there was a savings of $36,479.
Conclusions: SBIRT with medical inpatients has potential to improve outcomes and reduce costs by reducing medical admissions and ER visits and increasing SUD, psych, and primary care utilization. Further research with a control group is indicated.
Financial Support: Christiana Care Community Services and Education Grant; NIDA U10 DA-13043 and KO5 DA-17009 (George E Woody, P.I)

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USING APPRECIATIVE INQUIRY TO IDENTIFY ADDICTION TREATMENT FIELD BEST PRACTICES AND PRIORITIZE FUTURE GOALS FOR COLLABORATIONS WITH KEY COMMUNITY STAKEHOLDERS.

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Aims: Examine previously effective collaborations within Virginia's substance use disorder prevention, treatment, and recovery field; Identify strategies to enhance longstanding and new partnerships; and Achieve nine action areas identified for leading the addiction studies field in Virginia.
Methods: Appreciative Inquiry is an approach to organizational change that uses an iterative cycle for identifying areas for action. In this qualitative study, thirty-eight individuals who were instrumental in shaping Virginia's addiction treatment field during the past 10 years participated in structured interviews. Participants were asked to respond to a series of questions in which they 1) provided details about their contribution, the contribution of others, aspects of the environment that made collaboration possible, and the resulting benefits of that collaboration to consumers; and 2) highlighted the most compelling trends that the addiction treatment field must address in order to provide and support effective services.
Results: Thirty-five interviews were completed, through which the following trends were identified as necessary for maintaining the effectiveness of Virginia's addiction field: 1) implementing evidence based practices; 2) extending the continuum of care through the lifetime; 3) embracing multiple paths to recovery and peer support services; 4) adapting to changing treatment populations, advancing technologies, and medical knowledge; 5) establishing partnerships with the criminal justice system; and 6) responding to new challenges in training and workforce development.
Conclusions: Using the Appreciative Inquiry process, stakeholders identified nine strategic opportunity areas that reflect emerging trends in the addictions field, changing roles of addiction treatment professionals, and visions for the future of the field. Action teams translated finding into objectives for leading the addiction field in Virginia forward.
Financial Support: Funded by the Mid-Atlantic ATTC SAMHSA/CSAT grant # 5UD1TI013415-09

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CHILDREN OF TREATED SUBSTANCE-ABUSING MOTHERS.

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Aims: Aim: Abuse of alcohol and illicit drugs causes serious health problems for mothers and their children. We examine mothers and their children approximately 10 years after admission to drug abuse treatment at which time these women were either pregnant or had children under 18.
Methods: Methods: These subjects (n=334) were recruited at admission to 44 treatment programs in 13 California counties during 2000-2002. Addiction severity index was administered at both intake and follow-up. Child functioning data were collected using the Child Behavior Checklist for ages 6-18 (CBCL).
Results: Results: Mothers' mean age was 40 (SD=7.5), predominately white (55.4%) or Hispanic (22.2 %), 35.9% did not complete high school, most were never married (32.5%) or divorced (28.0%), only 33.5% were employed, and 61.7% received public assistance. About 37.8% reported methamphetamine being their primary problem, followed by alcohol (20.4%), heroin (14.4%), cocaine (9.0%), marijuana (7.8%), and with 10.5% reporting other drugs. Most women (85.6%) reported a history of arrest. At the follow-up, few women reported drug use but many reported medical problems (ASI severity=0.33) and psychiatric problems (ASI severity=0.22; 46.1% having trouble understanding, 39.6% had serious anxiety, 26.5% serious depression). On average, women had 2.4 (SD=2.2) children under age 18, while 21.3% reported that children lived with others by court order and 19.2% had parental rights terminated. Relative to other drug types, children of mothers abusing cocaine or marijuana demonstrated poorer functioning with regard to rule-breaking and externalized behaviors.
Conclusions: Conclusions: Despite of mothers' drug abuse histories, these children (if stayed with their mothers) appear to be able to function normally.
Financial Support: Supported by NIDA R01DA021183, P30DA016383, & K05DA017648 (PI: Hser)

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CAFFEINATED ENERGY DRINKS IN COLLEGE STUDENTS LINKED TO HIGHER LEVELS OF ALCOHOL, MARIJUANA AND TOBACCO USE.

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Aims: There has been a dramatic increase in the sales of caffeinated energy drinks in recent years (Heckman, 2010) with escalating popularity among college students (Obrien, 2008). Consumption of these beverages has been linked to increased risk for alcohol-related problems, particularly in young adults (Arria et al. 2011). The purpose of this study was to determine if energy drink use was correlated with different patterns of alcohol and other substance use in an urban university setting.
Methods: 89 students from a mid-Atlantic, urban university were surveyed using an IRB-approved, anonymous, paper and pencil survey.
Results: Participants were 22.3 (±3.1) years old, 57.3% female and mostly Caucasian (59.6%). The majority of participants (65.1%) were seniors in college who lived in off campus housing (77.5%). Of those, 25% reported consuming at least one energy drink in a typical week (energy drink users=ED). ED were not significantly different in most demographic categories from the non-energy drink consumers (NED). However, there was a significant difference in the gender distribution between the two groups with 65.2% of the female respondents being NED, while 68.2% of the male respondents were ED. Energy drink use was correlated with higher levels of alcohol, marijuana and tobacco use. ED reported consuming a significantly higher number of drinks for both weekday ($p=0.015$) and weekend day drinking ($p=0.037$). They also consumed 5 or more drinks within a 2 hour period on significantly more occasions in the past month than NED ($p=0.021$). ED were also significantly more likely to report using marijuana both in the past month ($p=0.030$) and in the past year ($p=0.046$). Additionally, the frequency of smoking was significantly higher ($p=0.019$) in the ED.
Conclusions: There is a disturbing correlation between energy drink use and increased substance use in college students. The data from the current study suggest that more research must be done to understand this relationship and develop interventions to address the constellation of adverse health behaviors.
Financial Support: Non-funded research

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AFFECTIVE INSTABILITY PREDICTS PATHWAYS TO ALCOHOL AND MARIJUANA USE DISORDERS IN YOUNG ADULTS.

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Aims: We hypothesized that affective instability, as indexed by measures of depression (DEP), impulsivity (IMP), borderline personality disorder (BPD) traits and negative affectivity (NA), predict alcohol (AL) and marijuana (MJ) use problems in 399 young adult subjects, aged 18-25 years.
Methods: 131 participants met criteria for alcohol dependence (AD; +/- other drug dependence; DD), 50 had DD but not AD, 73 had AL abuse +/- other drug abuse, and 146 had no evidence of any substance use disorders. Assessment measures were: SCID II, Beck Depression Scale, Eysenck and Multidimensional Personality Questionnaires, and SSAGA.
Results: Structural equation modeling (SEM) revealed that that BPD traits predicted both AL and MJ problems, but this effect was mediated to a great degree by IMP. DEP symptoms also predicted both AL and MJ problems, but this effect was mediated to a great degree by BPD traits. NA also predicted AL and MJ problems, but this effect was mediated entirely by BPD traits. Finally, full SEM path modeling (BPD, IMP, DEP and NA predicting ALC and MJ) revealed significant independent predictive paths from: (1) BPD traits to both AL and MJ (std betas = .17 and .21), (2) IMP to both AL and MJ (std betas = .31 and .20), and (3) DEP symptoms to both AL and MJ (std betas = .24 and .20). NA was not significantly associated with AL or MJ. BPD, IMP, DEP, and NA were all strongly correlated (rs .28 to .68).
Conclusions: Broadly, these results provide evidence of affective regulation problems in early onset substance use disorders. These traits appear to be associated with externalizing problems such as IMP and substance use disorders. We speculate that the BPD-related effects are likely driven by affective instability and problem dynamics seen in intense, unstable relationships, rather than self-injury. Such traits could serve as potential therapeutic and preventive targets for substance use disorders.
Financial Support: AACAP and NIDA's Physician Scientist Program in Substance Abuse (K12 DA000357), NIAAA (R01AA013650) and NIDA (R01DA017924).

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EXPOSURE TO ALCOHOL DURING ADOLESCENCE OR ADULTHOOD ALTERS THE REWARDING EFFECTS OF COCAINE IN ADULT RATS.

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Aims: Alcohol is one of the most commonly used drugs during adolescence, and may cause long-term behavioral and neural effects which persist into adulthood. However, little work has examined the long-term effects of adolescent alcohol exposure on the response to other drugs in adulthood. The present study examined the effects of adolescent alcohol exposure on the rewarding effects of cocaine in rats as measured with the conditioned place preference design. To determine if effects were due to the adolescent developmental period, the same procedure was replicated in adults.
Methods: Male rats were exposed to alcohol (2 g/kg) or vehicle for 10 days (PND 30-39 or 70-79). On PND66 or 106, baseline preferences were determined by allowing animals 15 min drug-free access to the entire conditioning apparatus. On the next day (Day 1), animals were administered either drug (5, 10 or 20 mg/kg cocaine, IP) or saline and confined to one of the conditioning chambers for 30 min. On Day 2, animals received the opposite injection and were confined to the chamber opposite that of Day 1. This 2-day sequence constituted one cycle, and conditioning consisted of four cycles over 8 days. On the day after conditioning cycle 4, a final preference test (15 min exposure to the entire apparatus) was conducted.
Results: Animals exposed to alcohol during adolescence and conditioned with 10 mg/kg cocaine significantly increased time spent on the drug-paired side when compared to baseline, while vehicle-exposed animals showed a preference only at 20 mg/kg cocaine. There were no significant differences between groups in time spent on the non-preferred side during either baseline or the preference test. Similar results were seen with animals exposed to alcohol during adulthood, indicating that the effect is not due solely to the period of ethanol exposure.
Conclusions: Exposure to alcohol during adolescence or adulthood may sensitize the rewarding effects of cocaine in adults. Such an increase could indicate a higher abuse liability following adolescent alcohol exposure.
Financial Support: This work was supported by a grant from the Mellon Foundation to ALR.

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REGIONAL DIFFERENCES IN THE ROLE OF THE VTA ON HEROIN-INDUCED CONDITIONED IMMUNOMODULATION.

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Aims: Heroin use has been shown to suppress several immune parameters that are important to the innate immune response. Previous studies in our laboratory have shown that these effects of heroin on immune function can be conditioned to environmental stimuli. Recently, we have demonstrated that these conditioned responses are mediated via a circuit that exists between the nucleus accumbens and basolateral amygdala. Furthermore, stimulation of D1 dopamine receptors within these brain regions is necessary to produce heroin-induced conditioned immune suppression. The current study investigates the role of the ventral tegmental area (VTA) on heroin-induced conditioned immunomodulation.
Methods: The conditioning procedure consisted of repeated pairing of heroin (1 mg/kg) administration with placement into a distinctive environment. On test day, animals (n=24,22) received bilateral intra-VTA microinfusions of a mixture of the GABA agonists baclofen/muscimol (0.03 nmol/0.3 nmol) to temporarily inactivate the rostral or caudal region of the VTA prior to re-exposure to the conditioned stimulus (CS). Following removal from the CS, animals received an injection of lipopolysaccharide (LPS) to induce an immune response. Spleen tissue and blood were collected six hours following LPS injection. Real-time RT-PCR was conducted to measure cytokine expression and nitric oxide production.
Results: Results indicate that inactivation of the rostral, but not caudal, VTA blocked the suppressive effects of the heroin-associated CS on nitric oxide production and on the expression of the proinflammatory cytokines, TNF-α and IL-6, in spleen tissue.
Conclusions: These data demonstrate that the rostral, but not caudal, region of the VTA is involved in heroin-induced conditioned immune suppression and further elucidate the neural circuitry involved in these conditioned effects.
Financial Support: This work was supported by grant DA25667 from the National Institute on Drug Abuse. Lee Hutson was supported by the National Institute on Drug Abuse Predoctoral Training in Research on Drug Abuse Grant (DA 007244-21).

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DIVERSION OF BENZODIAZEPINE THROUGH HEALTHCARE SOURCES.

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Aims: Prescription drugs, including benzodiazepines (BZ), are often diverted from the healthcare system to illegal sources. The present study examines the diversion of BZs via healthcare-related diversion sources, and how utilization of healthcare diversion sources is related to heavy BZ use and dependence.
Methods: Cross-sectional data were collected from five different groups of prescription drug abusers: methadone-maintenance clients (n = 239), active street drug users (n = 238), public treatment clients (n = 246), private-pay treatment clients (n = 173), and men who have sex with men (MSM; n = 185). Using computer-assisted personal interviewing procedures, participants' prescription drug use and diversion sources were assessed.
Analyses: Bivariate logistic regression models were conducted to examine correlates of healthcare diversion utilization.
Results: The most commonly reported healthcare diversion source in the last 90 days for BZ users was regular doctor, with 21% of the sample misusing their regular prescriptions. The mean number of times that each healthcare diversion source was used was highest for pharmacist than any other healthcare source; and the median number of pills obtained was highest for doctor shopping than any other healthcare source.
Findings suggest that younger and non-Hispanic White participants, private-pay clients, those who are insured, and those with high income were more likely to utilize healthcare diversion sources than those who were not. Heavy BZ users and those who were BZ dependent were more likely to report using a healthcare source to obtain BZs than light BZ users.
Conclusions: Participants reported going to healthcare sources less often, but they obtained more pills through these sources than through non-healthcare sources.Prevention of prescription drug use and diversion should target pharmacists and physicians, including educational programs regarding the typical profile of a diverter.
Financial Support: This research was supported by NIH Grant 5R01DA021330.

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FETO-MATERNAL OUTCOME OF PREGNANCY IN WOMEN MAINTAINED ON METHADONE BUT USING ILLICIT SUBSTANCES.

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Aims: To investigate the outcome of pregnancy in women maintained on methadone, I documented outcome variables from a cohort of pregnant opiate dependent women (n=30), on methadone maintenance therapy. The aim was to identify the obstetrics and neonatal characteristics of such pregnancy and the level of contact with services via antenatal visits and to investigate and document the relationship between levels of contact, the continued use of illicit substances and pregnancy outcomes.
Methods: The study type is a retrospective descriptive analysis of data.
Results: . The mean birth weight was 2798.6gms. It was below the 10th percentile and comparable to reports in other studies. There were statistical significant associations between birth weight and use of illicit drug and between use of illicit drugs and gestational age (crack use and length of labour r2 =.57 and r2 = .012. P = 0.05; Cocaine use and type of delivery r2 = .515 and r2 = .006. P = 0.05; Birth weight and length of gestation r2 .429 and r2 = .041. p= 0.05).
There were also statistical significant association between methadone and blood loss during pregnancy as well as statistical significant association between antenatal attendance, birth weight and length of gestation (methadone maintenance and blood loss in labour r2 = .587 and r2.021. p = 0.05; Antenatal visits and apgar's score r2 = -.962 and r2 = -038. p = 0.05; antenatal visits and gestation r2 =.504 and r2 = .033. p = 0.05).
Conclusions: This confirms that methadone maintenance therapy is good for pregnant opioid dependent female
Financial Support: Internally sponsored.

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PERCEIVED BARRIERS TO SUBSTANCE ABUSE TREATMENT AMONG ASIANS AND PACIFIC ISLANDERS.

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Aims: To conduct a 3-site qualitative study involving interviews of API drug users enrolled and not enrolled in drug abuse treatment, treatment providers familiar with treatment of API populations, and key community informants, in order to identify barriers and facilitators to substance abuse treatment entry among Asians and Pacific Islanders (APIs).
Methods: This NIDA Clinical Trial Network study was conducted in San Francisco, CA, Los Angeles, CA, and Hilo, Hawaii. Treatment counselors (n=60), and API drug users enrolled in treatment (n=80) were recruited from drug treatment programs known to specialize in care of API populations. API drug users not enrolled in treatment (n=45) were recruited through snowball contacts by peers and by outreach. Key informants (n=30) were nominated by participants. A semi-structured interview was utilized to identify barriers and facilitators to drug abuse treatment entry for API drug users. Interviews were digitally recorded and transcribed. A coding book was developed and refined using a small sub-sample of interviews, initial inter-rater reliability was determined to be approximately 85%, and data were thematically examined.
Results: Interviews with participants identified major thematic groupings associated with barriers and facilitators to substance abuse treatment entry including church/spiritual beliefs, psychological factors, family, law enforcement, language, culture, and financial concerns.
Conclusions: Program staff, substance abusers, and key informants expressed a need to address API cultural issues, in particular, the role of the family and church as both facilitator and impediment to substance abuse treatment entry. Our study highlights the need to develop culturally-tailored interventions designed to increase access to and engage APIs in substance abuse treatment.
Financial Support: Supported by: NIDA Grants (U10DA15815, U10DA13045, U10DA013036, P50DA009253)

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RATES OF SUBSTANCE USE IN DENTAL CLINIC PATIENTS.

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Aims: Drug use/abuse is associated with a number of physical health consequences, including poor dental health. The existing research on the prevalence of drug misuse in dental settings is preliminary. The limited available data indicate that the prevalence of substance use in free or low-income dental clinics is 3-4 times higher than the general US population. The present study described the prevalence of problematic alcohol use, illegal drug use, and prescription opioid misuse in a large University Dental clinic providing low-cost services to adults in the community.
Methods: For this study, research staff recruited 389 patients from the waiting area of University of Michigan Dental School Clinic during a 5 week period. During recruitment, 86% of patients who were approached consented to participate in this study.
Results: Overall, 44.2% of the sample reported either extra-medical use of prescription opioids or use of an illegal drug in the past 3 months. Over 37% of the sample reported extra-medical prescription opioid use. Other common substances of misuse included marijuana (15.9%), amphetamines (4.4%), 'street' opioids (2.6%) and cocaine (2.4%). Combining responses related to these non-prescription drugs, 19.0% of participants reported some illegal drug use in the past 3 months. Additionally, 39.2% of the sample reported alcohol use on the Alcohol Use Disorders Identification Test (AUDIT) that exceeded a cut-off of 9 as a conservative marker of alcohol-related problems.
Conclusions: Overall, these results highlight the high prevalence of substance use and/or misuse in patients seen in a dental school clinic. In addition to illicit drug use, misuse of prescription pain medications is common. These findings suggest that dental clinics are an appropriate setting for interventions designed to identify and offer interventions for at-risk substance use patients.
Financial Support: This project was supported with pilot funds from the Department of Psychiatry at the University of Michigan.

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ALCOHOL AND OTHER DRUG USE ACROSS INTERNATIONAL BORDERS.

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Aims: Knowing the reality of alcohol and other drugs use among young people in festive places on the two sides of the French/Spanish boarder is helpful to clinicians. This report deals with the harm reduction strategies known and used by these young people.
Methods: This was a qualitative study: 50 detailed interviews with young French and Spanish people were analyzed, as well as several other groups involved in this field: mental health professionals, parents, restaurants and bar managers, street educators and civil monitors. These interviews gave an internal view of drug consumption in this international border area.
Results: Alcohol consumption is widely tolerated, with no respect to the law that forbids alcohol selling to persons under 18, in France as in Spain. The youngest drink in the street and begin with marijuana use. Later, they use private places ("garages") and after, bars, pubs and finally nightclubs. During consumption, there is no difference between males and females. Young French are moving to Spanish festive places due to local characteristics of nightlife. Alcohol use is more likely linked to weekends whereas marijuana appears to be used daily. Alcohol and other drugs are used in a compulsive way by young French, in a short time, and they lose control. This binge use often leads to aggressiveness and violence. Drugs also seem to be often mixed so as to get precise and immediate effects. Nevertheless, these young people don't recognize the harms linked to this drug mix.
Conclusions: Local and specific actions will be proposed according to the conclusions of this study.
Financial Support: French

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GENDER DIFFERENCES IN EXERCISE PATTERNS FOR PERSONS ENROLLED IN COMMUNITY-BASED SUD TREATMENT AND RECOVERY PROGRAMS.

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Aims: SUD treatments often yield modest effects. Strategies to improve outcomes & prevent relapse are important, especially for women. A promising therapeutic adjunct may be exercise. Exercise is associated with decreased craving & increased abstinence rates in cigarette smokers; few published studies have examined effects of exercise on recovery from other drugs. This study compared attitudes toward & knowledge about exercise & current exercise practices in men & women with SUDs.
Methods: Participants (N=205) recruited from CTN-affiliated residential & outpatient SUD programs & a community peer-support recovery site. Interactive ACASI program was used to administer anonymous surveys for demographics, substance use, exercise knowledge & behavior & nutrition. Chi-squares & t-tests analyses were used to identify gender differences in beliefs about exercise & patterns of physical activity.
Results: In preliminary analysis, men participated in exercise more often than women (63.2% vs 42.3%). Men more likely to report engaging in both moderate (63.2% vs 42.5%) & vigorous (44.8 vs 23.1%) exercise on at least a weekly basis more often than women. Men rated exercise as playing a more important role in their recovery from SUDs than women (78.4 vs 65.4%).
Conclusions: Findings show men engaged in more vigorous & frequent exercise than women. In addition men more likely to view exercise as playing a substantive role in recovery. Cause & effect relationships cannot be imputed from such correlations, findings nonetheless suggest women may experience greater barriers to physical activity and warrant further study. In particular, researchers should be alert to such gender differences in the design of studies targeting exercise & SUD treatment.
Financial Support: VCU IWH Seed Grant, U10DA13034

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WHAT DOES SELF-IDENTIFIED DRUG OF CHOICE TELL US ABOUT CRIMINAL OFFENDERS?

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Aims: The phrase "Drug of Choice" (DOC) refers to a substance abusers preferred drug. This information often adds to the clinical picture of the patient, because substance abusers are often polysubstance dependent. Individuals who differ in terms of their DOC have been shown to differ on characteristics such as age, race, marital status and psychiatric illnesses. No such correlations exist with DOC and criminal justice involvement.
Methods: The participants (N=19,666) of a community correction setting were separated by DOC (alcohol, marijuana, cocaine, and opiates) and four separate binary logistic regression analyses compared each DOC to a group of the other 3 DOCs.
Results: The results indicated that among community correction population, Alcohol as DOC was associated with being older, White, male, living alone, not being unemployed or disabled, having private health insurance, being medicated for a mental problem, and having a criminal history of person offenses, but not property court or substance offenses. Cocaine as DOC was associated with being older, Black, female, attempting suicide, not being single, having less than a high school education, living in a shelter or with relatives, being unemployed, not having health insurance or being on government health insurance, being physically and sexually abused, and committing property and court offenses but not person offenses. Marijuana as DOC was associated with being younger, Black, male, not attempting suicide, never having been married, not living in a shelter or with relatives, not being unemployed, not being without health insurance, not taking medication for a mental problem, and committing substance but not property or court offenses. Opiates as DOC was associated with being White and female, being married, being more educated, being unemployed, not having health insurance, being medicated for mental problems, not being physically abused, and not reporting a criminal history of person offenses.
Conclusions: Overall, these findings are consistent with and extend the literature on DOC.
Financial Support: Supported by UAB Psychiatry Departmental Funds.

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ROLES OF HIPPOCAMPAL AND AMYGDALAR CAMP AND CGMP IN EXTINCTION OF COCAINE-INDUCED CONDITIONED PLACE PREFERENCE.

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Aims: Several phosphodiesterase (PDE) inhibitors improve cognition, suggesting that increases in brain levels of cAMP and cGMP facilitate learning and memory. The present study investigated the efficacies of the PDE10A inhibitor papaverine, the PDE4 inhibitor rolipram, and the PDE9 inhibitor BAY-73-6691 in the consolidation of extinction learning of cocaine-induced conditioned place preference (CPP).
Methods: To investigate the effect of the PDE inhibitors on brain levels of cyclic nucleotides, naïve B6129S male mice received papaverine (10mg/kg), rolipram (0.05, 0.25, 1.0mg/kg), BAY-73-6691 (0.03, 0.3, 3.0mg/kg) or saline. The hippocampus and amygdala were extracted after 30 min and cyclic nucleotide levels were determined. For CPP studies, mice were conditioned by escalating doses of cocaine (3,6,12 and 24mg/kg). For extinction training, mice where exposed daily to the conditioning context (20min) in the absence of cocaine. Immediately following each extinction session, mice received a) saline, b) papaverine (10mg/kg), c) rolipram (0.25mg/kg) or d) BAY-73-6691 (3mg/kg) and were returned to the home cage. Extinction rates were recorded daily.
Results: Papaverine significantly increased hippocampal and amygdalar cyclic nucleotides. Rolipram and BAY-73-6691 dose-dependently increased cAMP and cGMP levels, respectively, in the hippocampus and amygdala. Mice that received saline injections following the extinction sessions maintained CPP for >7 days. Mice that received papaverine and BAY-73-6691 showed significant acceleration of CPP extinction. These treatments also attenuated the reinstatement of CPP. Rolipram, however, had only a minor effect on extinction.
Conclusions: Results suggest that increases in hippocampal and amygdalar cGMP levels have a more prominent role in the consolidation of extinction learning than increases in cAMP levels. PDE inhibitors that selectively increase brain cGMP levels may be beneficial for extinction learning.
Financial Support: Supported by R01DA026878 and R21DA029404

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ADDICTION TREATMENT MATCHING IN THE 21ST CENTURY: A NEW SOLUTION TO AN OLD PROBLEM.

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Aims: There are an estimated 24 million Americans who meet criteria for substance dependence, only 10% enter treatment annually (SAMHSA, 2010). An additional 1.1 million indicate that they need treatment but didn't receive it, and nearly half of those report making an effort at treatment entry but being unsuccessful. Some of the most commonly cited barriers to successful treatment entry include lack of access to reliable information and stigma. Our aim is to test the utility of an automated, algorithm driven, online treatment-matching system that improves access.
Methods: We developed an online addiction-treatment system consisting of: 1) A screening form, 2) a set of research-informed matching algorithms that map user input onto provider variables, and 3) a national database of addiction-providers based on SAMHSA's publicly available national database. The tool has been made available to online treatment seekers and data collected includes demographic variables (e.g., age, gender, race/ethnicity, location), drug use, mental health information, and previous addiction treatment experience.
Results: We present data from 529 completed online searches that indicate a broad range of characteristics including age (M = 33.8, Min = 14, Max = 70), available funds for treatment (M = 3867, Min = $0, Max = $60,000), and drug use characteristics. We also present a number of specific case examples of matching based on users supplied data to highlight the strengths and limitations of the current system.
Conclusions: Findings from this preliminary research support the utility of a widely accessible, online, treatment matching system to facilitate successful treatment seeking. This system's ability to provide low-cost and yet highly targeted treatment recommendations to a national population, and the implications of this for possible improvements in treatment success, are presented and discussed.
Financial Support: Financial support for this research was supplied by California Treatment Services.

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THE EFFECT OF METHAMPHETAMINE ON GREY MATTER STRUCTURE IN THE HUMAN BRAIN USING VOXEL-BASED MORPHOMETRY.

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Aims: The effect of methamphetamine (MA) on the structure of the human brain has been studied mainly in abstinent individuals. Previous studies have reported global reductions in grey matter (GM) in abstinent MA-dependent subjects, particularly in cortical GM volume relative to healthy controls, as well as an increase in striatal volume suggesting the occurrence of a compensatory mechanism in the dopamine-rich basal ganglia. Decreases in GM density have also been reported in the right middle frontal gyrus, left middle frontal gyrus and bilateral insula. GM density in the left superior frontal gyrus was negatively correlated with performance on a behavioural measure of impulsivity.
Methods: 17 currently MA-dependent and 20 healthy control subjects aged 18-46 years were scanned in a Siemens Magnetom Avanto 1.5T MRI scanner. Two high-resolution T1-weighted anatomical scans were acquired for each subject using an MPRAGE sequence. The scans were averaged and analysed for differences in voxel-wise GM volumes using voxel-based morphometry (FSL-VBM). Two-tailed unpaired t-tests, co-varied for age and gender, were performed using FSL-Randomise. FSL's SIENAX tool was used to analyse global brain, GM and white matter volumes.
Results: Normalised global volumetric measures of total brain, GM, white matter and peripheral GM did not differ between groups. However, the FSL-VBM analysis revealed a significant reduction of GM (27.1%, $p<0.001$) in the left superior frontal gyrus (SFG) in MA-dependent subjects compared to controls.
Conclusions: This is the first study to investigate structural GM differences between current users of MA and healthy controls. There was a significant reduction in GM volume in the left SFG in current MA users in comparison to healthy controls. It is possible that GM reduction in the other brain areas previously reported in the literature only occur following abstinence from MA.
Financial Support: The School of Pharmacy, The University of Auckland

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ASSOCIATION BETWEEN CHRNA5 GENETIC VARIATION AND BRAIN REACTIVITY TO SMOKING IMAGES IN WOMEN SMOKERS.

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Aims: Tobacco smoking is the leading preventable cause of death in the developed world. To prevent and treat smoking addiction, we must develop a more comprehensive understanding of risk factors associated with smoking maintenance and dependence. Genome wide association studies identified a relationship between nicotine dependence and a single-nucleotide polymorphism (SNP, rs16969968) of the nicotine acetylcholine receptor (nAchR) alpha-5 subunit gene (CHRNA5). This SNP leads to an aspartate to asparagine mutation at the 398th amino acid (Asp398Asn) and it is unknown whether smoking cue reactivity is moderated by this genetic variation.
Methods: We assessed the role of rs16969968 on brain functional MRI (fMRI) reactivity to smoking cues in nicotine dependent women with (N=14) or without (N=10) the nicotine dependence risk allele. Smoking and other demographics for these 2 groups were equivalent (by Fagerstrom test for nicotine dependence, smoking pack-years, expired carbon monoxide levels, and age).
Results: Women without the risk allele showed greater fMRI reactivity to smoking images in brain areas related to memory and habitual behavior including hippocampus and dorsal striatum.
Conclusions: The mechanism by which rs16969968 moderates nicotine dependence remains unclear. However, the Asp398Asn polymorphism is associated with reduced nAchR function. We speculate that reduced nAchR function may disrupt memory, leading to relatively weaker smoking-cue associations. Although more studies are necessary to clarify the significance of these findings, these data suggest that smoking cue fMRI reactivity may be useful for further characterizing the influence of CHRNA5 genetic variation on smoking dependence.
Financial Support: Supported by DA19378, DA017324, DA014013, DA015116, DA022276 & DA15036.

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THE OBSESSIVE COMPULSIVE COCAINE SCALE: ASSESSMENT OF FACTOR STRUCTURE, RELIABILITY, AND CONVERGENT VALIDITY.

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Aims: The Obsessive Compulsive Drinking Scale (OCDS) was developed as an assessment tool for examining obsessive-compulsive features of alcohol craving. While this measure has been adapted to assess obsessive-compulsive features of craving in other addictive behaviors, it has not been specifically adapted for assessing cocaine use. The purpose of the present study was to modify and adapt the OCDS to create the Obsessive Compulsive Cocaine Scale (OCCS), a measure that specifically assesses the obsessive-compulsive features of cocaine-related thoughts and behaviors.
Methods: The OCCS consisted of the 14 items from the OCDS, modified to specifically address cocaine use in lieu of alcohol. The measure was administered to 192 volunteers participating in two separate pharmacological treatment trials for cocaine-use disorder. All participants were treatment-seeking males and females (18 to 65 years) who met DSM-IV criteria for cocaine dependence. Participants were administered the OCCS on two separate occasions (~1 week apart) prior to receiving medications.
Results: Confirmatory factor analysis of the OCCS revealed that a two-factor solution, with 2 items pertaining to use behaviors removed, provided the best fit for the data. The root mean square of approximation was equal to 0.06 and the Bentler's comparative fit index was equal to 0.96. Internal consistency (Chronbach's alpha) was .85 for both the obsession and compulsion factors and 0.91 for the total score. Test-retest reliabilities for the obsession and compulsion factors were 0.64 and 0.69 respectively, and 0.71 for the total score. When correlated with the Brief Substance Craving Scale and the Cocaine Selective Severity Assessment, Pearson correlations for the factors and total score ranged from 0.44 to 0.58 ($p < .01$ for all).
Conclusions: Overall, the results demonstrate that the OCCS is sufficiently consistent and reliable, with acceptable convergent validity.
Financial Support: DA016368 and DA019903

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ON THE RAPID DEVALUATION OF CONSUMABLE COMMODITIES IN COCAINE ADDICTS: CROSS-COMMODITY DISCOUNTING OF SEX VS. MONEY.

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Aims: Humans tend to discount consumable commodities (e.g., drugs) at higher rates than money. Bickel et al. (in press) disentangled the appeal of immediate cocaine from the devaluation of delayed cocaine by comparing cocaine addicts' single- (C-C & M-M) and cross-commodity (C-M & M-C) discounting rates for cocaine and money. Discounting was higher when cocaine was the delayed commodity irrespective of the immediate commodity, indicating that elevated rates of discounting cocaine are related to the rapid devaluation of delayed cocaine. This rapid devaluation may underlie the elevated rates of discounting for other consumable commodities. The current study extended Bickel et al.'s findings to the discounting of sex versus money.
Methods: The current experiment obtained discounting rates for equated quantities of sex and money in 25 treatment seeking cocaine addicts. Single (S-S & M-M) and cross-commodity (S-M & M-S) discounting procedures were used. The findings were then compared to those of Bickel et al.
Results: Participants discounted S-S ($p = 0.007$) more rapidly than M-M. When averaging across immediate commodities discounting rates were higher for delayed sex ($p<.001$) relative to delayed money. No significant effect of immediate commodity was obtained. These findings mirror those of Bickel et al.
Conclusions: Consistent with Bickel et al. the elevated rates of discounting for the consumable commodity (i.e., sex) seemed to be due to the rapid devaluation of delayed sex. Taken together, these findings suggest that consumable commodities are rapidly discounted because they do not retain their value when they are delayed.
Financial Support: This work was funded by NIDA Grant R01 DA 12997; NIDA Grant R01 DA030241-01; and the Wilbur Mills Chair Endowment.

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COGNITIVE BEHAVIORAL THERAPY AND SUBSTANCE-USING MINORITIES: A META-ANALYSIS.

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Aims: To systematically investigate the effectiveness of Cognitive Behavioral Therapy (CBT) in reducing substance abuse among racial minorities.
Methods: Scientific databases were utilized to identify quasi-experimental intervention studies in the U.S. published between 1990 and 2010 that assessed CBT's effectiveness with substance use disorders.
Results: Of the 176 articles retrieved in the search, sixty (60) Cognitive-Behavioral studies were reviewed, and thirty-five (35) were selected. Outcome variables included lower rates of substance use or abstinence. Of the selected studies, 74% did not provide information about sample racial breakdown. Among studies providing data on race, 70% had a White sample majority. Only one study provided information on CBT effectiveness across race. African Americans were significantly less likely to complete treatment than Whites (ES = .64; F (1,100) =5.7, p=.02). Four studies had a Black sample majority. These showed poor retention rates and modest effects in reducing substance use (ES= .13 to .36).
Conclusions: Preliminary results indicate CBT effectiveness in reducing substance use cannot be generalized to minorities due to the limited inclusion of these groups in research. These results support the conclusion that cultural competency may be lacking from studies on the effectiveness of CBT as a substance abuse intervention for minority populations, and suggest a potential direction for future research.
Financial Support: There is no financial support for this project.

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GENETIC DISSECTION OF INHIBITORY CONTROL ABILITIES IN MICE.

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Aims: Behavioral flexibility involves the ability to exert inhibitory control over impulsive actions. Behavioral inflexibility and impulsivity are characteristic of behavior addictions.
Methods: We investigated the genetic basis of individual differences in flexibility, measured using an operant reversal learning task. We quantified discrimination acquisition and subsequent reversal learning in a cohort of 51 BXD strains of mice, for which we have matched data on sequence, gene expression in key CNS regions, and neuroreceptor levels.
Results: Strain variation in trials to criterion on acquisition and reversal was high, with moderate heritability (~0.3). Acquisition and reversal learning did not covary at the strain level, suggesting that these separate learning traits are effectively under independent genetic control. Reversal performance did covary with D2 receptor levels in the midbrain, consistent with patterns of human D2-like receptor availability and measures of impulsivity. Reversal, but not acquisition, is linked to sequence variants on mouse chromosome 10 with a peak LRS of ~20 ($p < .05$ genome-wide) at genomic locus that encodes synapsin 3 (Syn3). Variance in mRNA levels in neocortex, hippocampus, and striatum supports a role of Syn3, as well as two linked genes (Nt5dc3 and Hcfc), in reversal learning.
Conclusions: This work demonstrates surprising trait independence and genetic control and illustrates how globally coherent data sets for a single family of strains can be interrogated and integrated to uncover genetic sources and molecular and neuropharmacological candidates of complex behavioral traits relevant to human psychopathology.
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DEFINING CLIENT OUTCOMES: A STUDY OF MINORITY-FOCUSED SUBSTANCE ABUSE TREATMENT STAFF.

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Aims: Underadoption of evidence-based treatments is a widespread problem in the field of substance abuse. Recently, the adoption of evidence-based treatment guidelines has been linked to the use of standardized assessments (e.g. Addiction Severity Index) in clinics (Rieckman et al., 2010). The present study examined discrepancies between perspectives of treatment providers and funders or researchers regarding important outcomes in minority-focused substance abuse treatment.
Methods: We conducted 22 semi-structured interviews with clinicians and directors at minority-focused treatment programs in San Francisco. Our sample consisted of two Asian American, African American, and Native American treatment centers, and one Hispanic and Lesbian Gay Bisexual Transgender (LGBT) treatment center. Each interview was audio recorded, transcribed, and coded independently by 2 researchers using Atlas ti software for analyzing qualitative data.
Results: Across programs, several themes emerged regarding the treatment staff's definition of internal (i.e., clinic specific) outcomes for the client. Internal outcomes considered important by treatment providers included cultivation of a family environment as well as emphasis on the client returning to receive more treatment and to give back to the program. These encourage formation of permanent ties with the treatment program. Treatment staff's understanding of external (i.e., funding specific) outcomes presented a similar concept of what outside agencies define as good outcomes. The idea of external outcomes not aligning with the treatment programs' internally-focused client outcomes was seen across all minority groups.
Conclusions: There are significant discrepancies in defined outcomes between practitioners and the research literature which may prevent the use of standardized assessments and impede future adoption of evidence-based practices. Future research should explore predictors of agreement between sectors which in turn could improve outcomes for clients.
Financial Support: Robert Wood Johnson foundation diversity supplement awarded to Dr. Larios (ID:65173)

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ARE PERCEIVED NEIGHBORHOOD ENVIRONMENT CHARACTERISTICS ASSOCIATED WITH THE LIKELIHOOD OF SMOKING AND ALCOHOL USE?

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Aims: The neighborhood environment has been shown to be related to health status and health-related behaviors. We examined whether perceived neighborhood characteristics, perceptions of neighborhood infrastructure and safety, were associated with smoking behavior and alcohol use.
Methods: Cross-sectional data from adults aged 18 and over, who were representative of the population in a US metropolitan Midwestern area (n=586, 69.8% women) were used to examine associations between perceived neighborhood environment characteristics, psychosocial characteristics, health behaviors (including smoking and alcohol use), and demographic characteristics. All data were assessed during a 60-minute structured interview onsite. Multiple regression analysis was used to explore independent associations between perceptions of neighborhood environment and health behaviors after adjusting for covariates.
Results: Participants with the negative perceptions of neighborhood safety (OR = 0.58; 95% CI = 0.36-0.92, $p < .05$) and those who were stressed (OR = 1.18; 95% CI = 1.09-1.27, $p < .001$) were significantly more likely to binge drink. Although perceptions of neighborhood infrastructure and neighborhood safety were not associated with the likelihood of smoking, participants who had more depressive symptoms were more likely to smoke (OR = 1.15; 95% CI=1.06-1.25, $p<.001$). However, participants who had negative perceptions on neighborhood safety reported having higher stress and depression than those who had positive perceptions ($p < .05$).
Conclusions: Perceived neighborhood environment characteristics were importantly associated with health behaviors. Approaches to reduce smoking and alcohol use may improve outcomes by expanding their focus to environmental attributes that are associated with those health behaviors.
Financial Support: National Institute of Diabetes and Digestive and Kidney Diseases grant# R01-DK064284; Poston, PI; National Institute of Drug Abuse grant# T32-DA007233-27.

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REPEATABILITY OF LABORATORY STRESSORS IN HEROIN USERS: EARLY VS. MID TREATMENT.

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Aims: Aim: To investigate the responsiveness to and repeatability of commonly used standardized laboratory stressors at two points in drug treatment.
Methods: Methods: The Paced Auditory Serial Addition Task (PASAT-C, a psychological stressor), and the cold pressor test (CPT, a physical stressor) were administered twice, approximately 1 month and 4 months after initiation of methadone maintenance (daily methadone and weekly individual counseling) in heroin users, on separate days in randomized order. Physiological effects and subjective responses were measured as change from baseline (post-test minus pre-test) and compared at the 1-month and 4-month time points.
Results: Results: At both 1 month and 4 months, the PASAT-C produced significant reductions in happiness (first: p=.003; second: p=.004) and significant increases in stress (first: p=.0001; second: p<.0001), difficulty concentrating (first: p=.009; second: p=.005) and frustration (first: p=.002; second: p=.003). The magnitude of these effects did not differ between the 1-month and 4-month PASAT-C sessions (happiness: p=.91; stress: p=.96; concentration: p=.79; frustration: p=.92). The CPT, at both 1 month and 4 months, produced significant increases in reports of stress (first: p=.012; second: p=.0006) and in heart rate (first: p=.003; second: p=.0007) and blood pressure (first: systolic, p<.0001, diastolic, p<.0001; second: systolic, p<.0001, diastolic, p<.0001). As with the PASAT-C, the magnitude of these effects did not differ between the 1-month and 4-month CPT sessions (stress: p=.29; heart rate: p.67; systolic: p=.38; diastolic: p=.31).
Conclusions: Conclusions: The PASAT-C and CPT induce subjective increases in stress, changes in affect, and changes in physiological measures in methadone-maintained outpatients. These effects do not diminish during the early months of methadone maintenance, meaning that the procedures should produce valid data in experimental designs that call for repeated measures across that time frame.
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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DIVERSION AND ABUSE OF BUPRENORPHINE: PHYSICIAN SURVEY.

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Aims: Diversion and abuse of substance abuse medications is a threat to their continued approval and development. One medication, buprenorphine, has restricted prescribing to certified physicians. These physicians may offer a perspective on in the diversion and abuse of buprenorphine as the availability of the medication has increased.
Methods: As a requirement for approval, the distributor was required to institute a risk management plan that included postmarketing surveillance conducted by an independent contractor. As part of it, surveys are sent to randomly selected certified physicians quarterly. From 2004-09, 8,966 surveys were completed. Physicians were asked if they had heard of sales of buprenorphine, the ease of obtaining it illegally relative to methadone and OxyContin, the reasons why individuals used it illegally, and sources. Availability was indicated by the number of tablets of Suboxone (over 90% of sales) distributed.
Results: From 2005-09 availability of Suboxone increased 1,651%. Awareness of street sales increased from 23% in 2004 to 46% in 2009. By 2009, 81% and 68% thought it was easier to obtain it illegally than methadone and OxyContin. The majority of physicians believed that patients in treatment for opioid dependence were the major source. They increasingly reported lax prescribing practices by physicians contributed to illegal diversion. Most physicians reported that the reasons for using buprenorphine illegally was to avoid withdrawal while awaiting treatment, not to get high.
Conclusions: Certified physicians increasingly report that buprenorphine is diverted and abused. In addition, physicians believe it has become easier to obtain than methadone or OxyContin. The motivation for its illegal use is to avoid withdrawal while awaiting access to treatment not to get high. Compared to availability, the increases are small. Nevertheless the increases merit continued monitoring and development of strategies to curtail diversion and abuse, such as increases in access to treatment.
Financial Support: This research was supported by a contract to CRS Associates from Reckitt Benckiser Pharmaceuticals, Inc.

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BASELINE DIFFERENCES IN RESIDENTS' ATTITUDES AND BEHAVIORS IN DELIVERING SBIRT SERVICES TO AT-RISK DRUG AND ALCOHOL USERS.

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Aims: Screening, brief intervention and referral to treatment (SBIRT) for risky drinking and drug use has been shown to be effective in reducing patients' use. Physician initiated brief interventions can be effective but difficult to implement and sustain in real world settings. This analysis examines barriers to implementing a physician-based SBIRT model by examining baseline differences in residents' attitudes and behaviors in addressing patients' risky drinking compared to drug use.
Methods: Consented residents (N=155)from four primary care residency programs were asked to complete a clinician questionnaire prior to initial SBIRT training. The questionnaire included separate but similarly worded questions for alcohol use and drug use behaviors. Paired sample t-tests and cross-tabs were used to identify differences between the alcohol use questions and the corresponding drug use questions.
Results: Residents reported more consistent screening for drug use behavior and more confidence in identifying the at-risk drug user when compared to the at-risk alcohol user. Residents also report being more comfortable discussing medications to aid in recovery from drug abuse and more confidence in prescribing these medications than prescribing medications for alcohol abuse or dependence. Likewise, they view medications as more important in the drug abuse recovery process than alcohol abuse recovery. A measure of residents' stage of change as related to addressing substance use issues found that residents are significantly further along the stage of change continuum for drug misuse than for at-risk alcohol use.
Conclusions: These findings suggest that residents view drug use as a more serious issue than at-risk alcohol use and are therefore more comfortable discussing this with patients and more knowledgeable about appropriate treatments. There is a significant need for SBIRT training, particularly training related to identifying and intervening with the at-risk alcohol user and the medications appropriate for treating alcohol dependent patients.
Financial Support: Supported by SAMHSA (TI1019545)

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HUMAN PSYCHOPHARMACOLOGY AND DOSE-EFFECTS OF SALVINORIN A, A KAPPA-OPIOID AGONIST HALLUCINOGEN PRESENT IN THE PLANT *SALVIA DIVINORUM.*

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Aims: Salvinorin A is a potent, selective nonnitrogenous kappa opioid agonist and the known psychoactive constituent of *Salvia divinorum*, a member of the mint family that has been used for centuries by Mazatec shamans of Mexico for divination and spiritual healing. *Salvia divinorum* has over the last several years gained increased popularity as a recreational drug. This is a double-blind, placebo controlled study of salvinorin A in 4 psychologically and physically healthy hallucinogen-using adults.
Methods: Across sessions, participants inhaled 16 ascending doses of salvinorin A and 4 intermixed placebo doses under comfortable and supportive conditions. Doses ranged from 0.375 μg/kg to 21 μg/kg. Subject-rated drug strength was assessed every 2 minutes for 60 minutes after inhalation.
Results: Orderly time- and dose-related effects were observed. Drug strength ratings peaked at 2 minutes (first time point) and definite subjective effects were no longer present at approximately 20 minutes after inhalation. Dose-related increases were observed on questionnaire measures of mystical-type experience (Mysticism Scale) and subjective effects associated with classic serotonergic (5-HT_{2A}) hallucinogens (Hallucinogen Rating Scale). Salvinorin A did not significantly increase heart rate or blood pressure. Participant narratives indicated intense experiences characterized by disruptions in vestibular and interoceptive signals (e.g., change in spatial orientation, pressure on the body) and unusual and sometimes recurring themes across sessions such as revisiting childhood memories, cartoon-like imagery, and contact with entities.
Conclusions: Under these prepared and supportive conditions, salvinorin A occasioned a unique profile of subjective effects having similarities to classic hallucinogens, including mystical-type effects.
Financial Support: Conduct of the study was supported by National Institute on Drug Abuse (NIDA) grant R01DA003889. Support for Dr. Prisinzano was provide by NIDA grant R01DA018151.

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NOVEL OPIOID RECEPTOR ANTAGONIST, ALKS 33, CO-ADMINISTERED WITH BUPRENORPHINE BLOCKS μ AGONIST EFFECTS.

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Aims: ALKS 33, a μ-opioid receptor antagonist with κ and δ agonist/antagonist activity is in development for the treatment of addictions. Buprenorphine (BUP) may be useful in the treatment of cocaine addiction and other disorders if administered safely to nonusers of opiates. We evaluated blockade of μ agonist effects of BUP by co-administered doses of ALKS 33. Pharmacokinetic (PK) and pharmacodynamic (PD) interactions were explored.
Methods: Subjects in our double-blind, placebo (PBO) controlled study were 12 infrequent users of opiates. Blockade was defined as no significant change between pre vs post BUP visual analog scale (VAS) self reports of high, good drug, liking and amount of post BUP miosis. With an adaptive dose strategy the first 6 subject cohort got ALKS 33, 1 mg or 4 mg or PBO with a simultaneous sublingual (SL) BUP 8 mg. Neither ALKS 33 dose produced complete blockade so a second 6 subject cohort received ALKS 33, 8 mg or 16 mg or PBO along with SL BUP. Safety and tolerability was assessed. ALKS 33 and BUP plasma levels were assayed by LC/MS/MS for PK analysis.
Results: BUP with PBO ALKS 33 produced substantial, but well tolerated, opiate PD effects. ALKS 33, at 1 and 4 mg doses, substantially diminished and at 8 and 16 mg abolished, BUP-induced miosis. ALKS 33 blockade of BUP subjective effects and miosis persisted during 24 hours post dose monitoring. No PK profile interactions were evident except small and variable increases in norbuprenorphine metabolite levels with ALKS 33 co-administration.
Conclusions: ALKS 33 simultaneously administered with a substantial dose of BUP produced rapid onset, long lasting, dose dependent blockade of BUP μ-opioid agonist effects. Co-administration of ALKS 33 and BUP was safe and well tolerated. The unique pharmacology of ALKS 33 plus BUP may represent a new treatment option in situations where blockade of BUP μ-agonist effects is desirable.
Financial Support: Financial support: NIDA N01DA-6-8867 and Alkermes Inc.

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TOPIRAMATE FOR THE TREATMENT OF COMORBID ALCOHOL AND COCAINE DEPENDENCE.

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Aims: The co-occurrence of alcohol and cocaine dependence is very common. Patients with both cocaine and alcohol dependence tend to have more psychosocial problems and worse treatment outcomes compared to patients addicted to cocaine or alcohol alone. Topiramate increases GABAergic activity and antagonizes the AMPA / kainate subtype of glutamate receptors. Through these two mechanisms of action, topiramate may reduce alcohol and cocaine reward and may reduce alcohol and cocaine craving. In previous trials, topiramate reduced alcohol use in alcoholics and reduced cocaine use in cocaine dependent patients. The current trial was intended to test the ability of topiramate to promote alcohol and cocaine abstinence among patients addicted to both alcohol and cocaine.
Methods: The study was a double-blind, placebo-controlled, trial involving 170 alcohol and cocaine dependent, patients. After achieving a period of abstinence from both drugs, patients were randomized to topiramate, titrated over 8 weeks to 300 mg daily, or identical placebo capsules. Medications were continued at full dose for 5 weeks. Patients also received twice weekly individual cognitive-behavioral relapse prevention psychotherapy. Primary outcome measures included alcohol use, measured by the timeline follow back, and cocaine use, measured by self-report and confirmed by urine drug screens. Secondary outcome measures included cocaine and alcohol craving, Addiction Severity Index results, medication compliance, cocaine withdrawal symptoms, and global improvement.
Results: Topiramate-treated patients were more likely than placebo-treated patients to be abstinent from cocaine at the end of the trial. Alcohol use declined in both groups but was not significantly different between groups. Complete results will be available at the meeting.
Conclusions: Topiramate plus cognitive behavioral therapy may reduce cocaine use in patients with comorbid alcohol and cocaine dependence.
Financial Support: This trial was supported by NIAAA grant R01AA014657.

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EFFECTS OF INTRA-ACCUMBAL ΔFOSB OVEREXPRESSION ON EXTINCTION OF OPIATE CONDITIONED PLACE PREFERENCE.

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Aims: ΔFosB accumulation represents a mechanism by which chronic exposure to drugs of abuse can alter gene expression and produce neural plasticity related to drug craving and relapse. This study examined experimentally induced ΔFosB protein overexpression within the nucleus accumbens and its impact on the extinction of morphine conditioned place preference in C57BL/6 mice.
Methods: One week prior to testing, mice were administered adeno-associated viral vectors expressing ΔFosB, JunD, or GFP bilaterally into the nucleus accumbens using stereotaxic surgery. Morphine (10 mg/kg sc) place conditioning consisted of five phases: pre-conditioned preference test (Day 1), conditioning (Days 2-9), post-conditioning preference test (Day 10), extinction (Days 11-14), and extinction preference test (Day 15). Mouse brains were removed three hours following extinction preference testing and immunoreactivity for ΔFosB/FosB protein was visualized.
Results: Intra-accumbal ΔFosB, but not GFP or JunD, viral vector administration significantly elevated ΔFosB/FosB immunoreactivity in the nucleus accumbens core following morphine place conditioning. Extinction training normalizes morphine CPP induction of accumbal core ΔFosB/FosB levels. Regression analysis revealed that only prelimbic ΔFosB/FosB immunoreactivity levels were a predictor of CPP difference scores in morphine conditioned mice after extinction training. Accumbal viral vector administrations did not alter ΔFosB in any other brain regions. Accumbal control viral vector administrations did not alter ΔFosB/FosB levels in any regions.
Conclusions: The present study suggests that ΔFosB/FosB levels in accumbens and prelimbic cortex are responsive to extinction of conditioned opiate approach behaviors.
Financial Support: Merit Award to GBK from the Department of Veterans Affairs

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PREDICTORS OF NON-PRESCRIBED USE OF PRESCRIPTION STIMULANTS, SEDATIVES, AND OPIOIDS.

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Aims: To examine whether traits representing reward or punishment sensitivity differentially impact non-prescribed use (i.e., misuse) of prescription stimulants, sedatives, and opioids.
Methods: Participants were 226 (67% female; 82% White) college students who completed:(1) a measure that assessed use during the past 12 months of prescription stimulants, sedatives, and opioids for non-prescribed purposes, (2) several facets of the Neuroticism and Extraversion scales of the NEO-PI; (3) the Anxiety Sensitivity Inventory; and (4) the Brief Sensation Seeking Scale (BSSS). Traits representing reward sensitivity were Experience Seeking (EXP-S) and Boredom Susceptibility (BS) from the BSSS and Excitement-Seeking (EXC-S) from the NEO-PI. Traits representing punishment sensitivity were Vulnerability to Stress (VTS) and Anxiety (ANX) from the NEO-PI and Anxiety Sensitivity. It was hypothesized that stimulant use would be better predicted by reward sensitivity, sedative use would be better predicted by punishment sensitivity, and opioid use would be predicted by traits representing both reward and punishment sensitivity. Hierarchical logistic regression analyses tested study hypotheses.
Results: Non-prescribed use of any prescription drug during the past 12 months was reported by 25% of the sample: 19.3% reported stimulant misuse, 7.8% reported sedative misuse, and 13.8% reported opioid misuse. Demographics were not related to misuse. Stimulant misuse was predicted by traits representing reward (Nagelkerke's R^2=.15, p=.003) but not punishment sensitivity (p=.09); stimulant misuse increased with EXC-S (OR=1.15, 95%CI=1.04,1.23, p=.008). Sedative misuse was predicted by traits representing punishment (Nagelkerke's R^2=.18, p=.003) but not reward (p=.11) sensitivity; sedative misuse increased with VTS (OR=1.30, 95%CI=1.10,1.60, p=.003). Opioid use was not significantly related to reward or punishment sensitivity (all p's>.05).
Conclusions: Campus prevention efforts should take into consideration the different characteristics of college students who misuse sedatives (i.e., anxious) *vs* stimulants (i.e., excitement-seeking).
Financial Support: Psychology Dept., Towson Univ.

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SYNTHESIS AND MONOAMINE TRANSPORTER AFFINITY OF 3-ARYL-3-ARYLMETHOXYTROPANE DERIVATIVES.

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Aims: A series of 3-aryl-3-arylmethoxytropane derivatives were found to exhibit potent affinity (nM) for serotonin transporters (SERT) in rat brain tissue. The aim of the present study was to synthesize and evaluate novel analogues to identify dual serotonin and dopamine transporter (DAT) affinity that could have potential use in the treatment of psychostimulant abuse.
Methods: The 3-aryl-3-arylmethoxytropane derivatives were synthesized via a four- or five-step process from 3-tropanone. The binding affinities at the SERT, DAT and norepinephrine transporters (NET) were determined by inhibition of [^{3}H]citalopram, [^{3}H]WIN 35,428 and [^{3}H]nisoxetine binding, respectively, in rat brain tissue.
Results: Over fifty 3-aryl-3-arylmethoxytropane derivatives were prepared. In general the analogues exhibited high affinity for the serotonin transporters, with good DAT affinity and poor NET affinity. The 3-phenyl-3-(3,4-dichlorophenyl)methoxynortropane congener was the most potent SERT ligand (K_i = 0.061 nM) and DAT ligand (K_i= 16 nM) of the series. The 3-aryl-3-arylmethoxytropane derivatives were generally SERT selective with DAT/SERT ratios ranging from 0.47 to 2,500.
Conclusions: These structure-activity studies indicate that the 3-aryl-3-arylmethoxytropane molecular scaffold is viable for the development SERT ligands with variable DAT affinity. With a broad range of DAT/SERT selectivity, the 3-aryl-3-arylmethoxytropane derivatives will be useful tools to explore the development of potential medications for psychostimulant abuse.
Financial Support: NIDA R01 DA011528

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EFFECTS OF PUNISHMENT ON SEEKING AND CONSUMPTION OF COCAINE AND WATER REINFORCERS.

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Aims: A defining characteristic of drug abuse is compulsive drug seeking, and continued use despite negative consequences. Here, we compared the effects of punishment on seeking of cocaine (COC) and water reinforcers in rats.
Methods: Both COC and water reinforcement groups, were required to "seek" the reinforcer by completing a fixed ratio (FR) to initiate a 2 hr reinforcer consumption period. The FR requirement progressively increased and/or decreased between sessions to measure the degree to which the animals would seek the reinforcer. During the consumption phase, COC (1.5 mg/kg/infusion) or water (0.03 ml/reinforcer) were available on a FR5 schedule with a 30 s timeout after each reinforcer presentation. The animals were tested on this procedure for 25 sessions. Beginning with test session 11, rats in the punishment groups received response contingent electric shock (1.0 mA, 2 s) substituted for COC and water reinforcers followed by two no shock days with usual COC and water reinforcement periods. This pattern of testing was repeated 5 times, such that rats were shocked on days 11, 14, 17, 20, & 23 with two no-shock test sessions following each shock day. Rats in no punishment control groups received no reinforcers (extinction) on the punishment days. There was no signal which differentiated shock from no shock test sessions during the seeking phase.
Results: Consumption responding for COC (n=5) and water reinforcers (n=5) was suppressed on shock test days. Rats in the COC (n=5) and water (n=6) no shock groups responded during the consumption period. Seeking in the punished water group was significantly suppressed compared to the no shock group ($p<0.05$). In contrast, seeking in punished COC reinforcer group was not suppressed compared to the no shock group. There was no difference in the level of seeking between the no shock COC and water reinforcer groups.
Conclusions: These results indicate that reward seeking in cocaine reinforced animals was less sensitive to punishment than reward seeking in water reinforced animals.
Financial Support: DA01058 and DA026600

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TIME OF DAY INFLUENCES VOLUNTARY INTAKE AND BEHAVIORAL RESPONSE TO DRUG AND FOOD REWARD.

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Aims: It is well known that time of day of external administration influences the response to drugs and natural rewards (Webb et al 2009), but the effect on self-administration is unclear. We developed a model allowing evaluation of time of day effects in reward anticipation, activity, and voluntary drug and food intake in sated animals.
Methods: Mice were housed in a 12:12 light-dark cycle (off-Zeitgeber time (ZT) 1200) with ad libitum chow. Mice (4 groups; 10/grp) received daily 1hr access to methamphetamine mixed in peanut butter (M+PB) or peanut butter alone (PB-alone) in early day (ZT 0400) or late day (ZT 1000). M+PB groups received alternating low and high concentrations of M during three 10-day blocks (45 or 90 μg M/g PB; equivalent to 2 or 4mg/kg if entire mixture eaten).
Results: Time of day effects were observed for both drug and palatable treat, with animals in the early day showing greater intake, anticipatory activity, and activity after ingestion. Interestingly, mice ingested twice the dose of methamphetamine in early day compared to late day (0.8mg/kg vs. 0.4mg/kg). When comparing rewards, M+PB vs. PB-alone groups differed in intake and activity after ingestion. PB-alone mice increased amount eaten over the 30-day study whereas M+PB mice showed stable intake according to concentration. In activity after ingestion, early day M+PB animals showed increased activity compared to the early day PB-alone group. However, late day M+PB animals showed no increase in activity following ingestion of methamphetamine when compared to late day PB-alone animals. A within-subjects replication of the entire study demonstrated similar results and revealed robust individual differences in preference for M+PB or PB-alone. Furthermore, diurnal variations in intake were observed for the preferred substances only.
Conclusions: The method used permits assessment of self-regulation of reward intake, is sensitive to individual differences, and distinguishes responses to drugs vs. palatable food. The empirical results indicate that time of day must be considered in assessing reinforcing effects of rewards.
Financial Support: NIH NS37919

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ESCALATING VS. BINGE METHAMPHETAMINE EXPOSURE REVEALS VULNERABILITY OF DOPAMINE REGULATION IN VENTRAL TEGMENTAL AREA.

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Aims: Chronic high doses of methamphetamine (METH) decrease striatal dopamine (DA), DA transporter (DAT), and tyrosine hydroxylase (TH). This study investigated how METH, delivered at sub-neurotoxic doses, affects DA-regulating proteins in both the nigrostriatal and mesoaccumbens pathways in order to better understand the early events leading to the escalation of use that ultimately contributes to METH-induced neurotoxicity.
Methods: Rats were injected intraperitoneally three times daily with either METH or saline. The first dose of METH was 0.1 mg/kg, and the dose was increased 0.1 mg/kg for each subsequent injection up to a dose of 4 mg/kg (i.e., the escalating regimen group). A third group of rats (i.e., the "binge" group) received three injections of METH over a single day at a dose of 4 mg/kg each. Two cohorts of rats were sacrificed either 48 hrs or two weeks following the last injection. The striatum (STR), substantia nigra (SN), ventral tegmental area (VTA), and nucleus accumbens (NAC) were dissected and analyzed for DA tissue content, total TH, phosphorylated TH, DAT, and the vesicular monoamine transporter 2 (VMAT2).
Results: No changes in DA tissue content were observed in the STR at either time point or in the SN at the 48 hr time point post-METH. In the NAC, DA tissue content decreased at the 48-hour time point even though ser 31 phosphorylation increased. In the VTA, both binge and escalating METH administration resulted in increased DA tissue content and TH protein. A striking reversal of the 48 hr effects occurred two weeks after METH administration, as DA tissue content decreased in the VTA and SN in the escalating group.
Conclusions: This initial increase followed by the subsequent decrease of DA tissue content in the VTA may contribute to craving for METH; thus, more METH may be taken in an attempt to restore DA to the higher levels, which may contribute to the toxic effects seen in the dopaminergic system in human addicts.
Financial Support: Funded by the Department of Pharmacology, Toxicology & Neuroscience at LSUHSC in Shreveport

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THE PREVALENCE OF THC AMONG DRIVERS IN A MEDICAL MARIJUANA STATE.

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Aims: In 1996, California voters passed Proposition 215 decriminalizing the cultivation and use of marijuana by chronically ill individuals. Since that time, at least 13 other states have passed similar legislation. In November, California citizens voted on Proposition 19, which not only decriminalized but also legalized marijuana. It did not pass, but 46.4% of citizens were in favor. Our research assesses the prevalence of Tetrahydrocannabinol (THC) among drivers residing in a medical marijuana state with and without a marijuana permit and examines the characteristics of those drivers, including their use of alcohol and other drugs.
Methods: Using procedures nearly identical with the 2007 National Roadside Survey, we interviewed a random sample of weekend nighttime drivers on Friday and Saturday nights at five data-collection sites in California; 819 drivers provided oral fluid samples. Of these, 8% tested positive for THC. Among those THC positive, men tested higher than women (Ms=.112 versus .045, p<.01), and young drivers also tested higher (OR=.959, p<.05).
Results: Having a permit for medical marijuana significantly predicted a positive THC test (p<.01). More drivers with a permit tested positive for THC (M=.44) than those without a permit (M=.07). Of the marijuana permit holders, almost all indicated using the permits. Further, permit holders reported using marijuana significantly more recently (M=1.2, between 24 hours and past 2 days) than nonpermit holders (M=3.4, between past month and past year) (p<.01). Among the THC users, 8.7% were THC abusers and 4.7% were THC dependent. Heavy drinking did not significantly predict a positive THC result.
Conclusions: It is not unexpected that the passage of such measures would significantly affect highway safety. Marijuana is, after alcohol, the most prevalent substance in drivers, both on the roads and in fatal crashes. Thus, the need for more information is crucial in this era of rapid law development and the limited knowledge about the risk that marijuana alone and combined with alcohol poses to driving.
Financial Support: NIAAA, NIDA

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COMMUNITY AND DRUG USE AMONG GAY MEN: THE ROLE OF NEIGHBORHOODS AND NETWORKS.

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Aims: A keen interest in "neighborhood health effects" research has emerged to better understand how residential contexts influence health outcomes independently of residents' individual characteristics. Despite mounting evidence regarding the role of neighborhood context for the health of residents from a variety of groups, hardly any neighborhood effects research has focused on gay men. Gay neighborhoods serve as vital places for gay men's social lives, yet few studies have examined their contributions to health. Yet, it is also important to recognize that gay community should not be viewed solely in the form of geographic community, particularly in light of the reported decline of gay neighborhoods. Gay social networks also play a critical role. Additionally, if gay neighborhoods are characterized by compositional and cultural features specific to gay life, then such neighborhoods should matter for the formation of social networks.
Methods: Drawing from theoretical perspectives on community and networks, we test hypotheses concerning whether gay neighborhoods and social network factors are associated with patterns of recent drug use among a sample of 740 gay men.
Results: Higher odds of drug use, particularly club drugs, were observed among individuals who resided in gay neighborhoods, had networks composed predominantly of other gay men and had increased socializing with gay men. Network factors did not mediate associations between gay neighborhoods and drug use.
Conclusions: This study highlights the importance of recognizing that two types of community contexts—neighborhoods and social networks—have implications for the health of gay men. In order to better understand and intervene upon the processes underlying the health risks faced by this vulnerable population, it remains imperative to move beyond a focus on individual-level factors and consider the role of the social contexts in which their health behaviors, such as drug use, take place.
Financial Support: No external financial support was used to complete this study.

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METHADONE WITH OR WITHOUT COUNSELING: IMPACT ON HIV-RISK BEHAVIORS.

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Aims: To examine the impact of routine drug counseling on changes in HIV-risk behaviors early in methadone treatment.
Methods: 230 newly-admitted methadone patients were randomly assigned to methadone without counseling (Interim Methadone [IM]; *n*=99) or standard methadone treatment with counseling (SM; *n*=131). All participants completed the Aids Risk Assessment at baseline (treatment entry) and at 4-month follow-up. A linear mixed model approach was used to analyze Treatment by Time changes in HIV drug- and sex-risk behaviors for the total sample; HIV drug-risk data for the subsample who reported injecting drugs in the 30 days prior to baseline (*n*=110); and HIV sex-risk data for the subsample who reported not using condoms in the 30 days prior to baseline (*n*=130).
Results: There were significant decreases in risky drug-use behaviors over time in both the total sample and the injector subsample, including frequency of injection, using dirty needles or works, and injecting with other injectors (all *p*s<.05). No significant Treatment X Time interaction effects were found for any risky drug use items in the total sample or the injector subsample. In the risky sex subsample only, there were significant decreases over time for frequency of sex without a condom (*p*<.05). No significant Treatment X Time interaction effects were found for any of the risky sexual behaviors in the total sample or the risky sex subsample.
Conclusions: Methadone treatment with or without counseling results in significant decreases in HIV-risk behaviors over time. No additional benefit to methadone alone was found on HIV-risk behaviors when routine drug counseling was added to methadone during the first four months of treatment.
Financial Support: National Institute on Drug Abuse 5R01DA013636-07

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FUNCTIONAL NEUROIMAGING OF THE SUBJECTIVE EFFECTS OF INTRANASAL D-AMPHETAMINE.

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Aims: This study used functional neuroimaging to examine the hypothesis that activation of catecholinergic brain regions associated with introspection is associated with the subjective effects of d-amphetamine.
Methods: A double blind, randomized within-subject design was used to examine the time course of effects of intranasal d-amphetamine (0, 32 mg) in 6 healthy female volunteers. d-Amphetamine solution was administered IN using a mucosal atomization device. A familiarization session was completed prior to 2 experimental sessions. Each session consisted of continuous VAS ratings of drug effect occurring before through 45 min after drug administration while functional brain images (BOLD) were collected with a Siemens Trio 3.0 Tesla magnet. Cardiovascular measures were also obtained. ANOVA was used to examine drug effects; linear regression (FSL) identified regions activated at the 2.58 threshold (p<.005); and hierarchical linear modeling is used to integrate the time-course data.
Results: Prototypical d-amphetamine-induced stimulant effects (e.g., significant dose- and time-related increases in VAS ratings, heart rate and blood pressure) were observed. Independent of VAS item, the left thalamus and putamen and the right lateral orbitofrontal cortex were more strongly activated during questionnaire completion following placebo, while the left insula, right mid-cingulate and temporal pole were more strongly activated following active drug. The left temporal pole was also activated with completion of selected VAS items (Stimulated, Feel Drug, Willing to Take Again) during active drug sessions, only. Ongoing analyses examine whether VAS ratings are associated with the magnitude of activation in these brain regions.
Conclusions: Brain regions associated with the interoceptive process vary as a function of drug condition and dimension being assessed. The temporal pole plays a prominent role in ratings of interoceptive dimensions associated with the positive effects of d-amphetamine.
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A RANDOMIZED TRIAL OF THE ADJUNCT USE OF D-CYCLOSERINE TO FACILITATE COGNITIVE BEHAVIORAL THERAPY OUTCOMES IN A COCAINE-DEPENDENT POPULATION.

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Aims: Cocaine dependence is a chronically relapsing disorder for which its predominant behavioral therapies are associated with only partial efficacy. The goal of this study was to determine if the N-methyl-D-aspartate (NMDA) glutamate receptor partial agonist and cognitive enhancer, D-Cycloserine (DCS), could boost the cocaine abstinence and treatment retention goals of cognitive behavioral therapy (CBT).
Methods: This study employed a placebo-controlled, randomized double blind trial design of 44 cocaine-dependent men enrolled in a 4-week outpatient Substance Abuse Treatment Program (SATP) at the Atlanta Veteran's Administration Medical Center. Subjects received 50 mg of DCS or placebo prior to four weekly sessions of a condensed version of a manual-based CBT for cocaine dependence. Cocaine abstinence and treatment retention measures represented primary outcome variables. Kaplan-Meier survival analyses for drug abstinence and treatment retention were conducted in SAS.
Results: Relative to a 12-step based treatment-as-usual, an under-dosed CBT was associated with significant improvements in drug abstinence and treatment retention at 4-weeks and for maintenance of drug abstinence after four more weeks of follow-up. The robust response to an under-dosed CBT was not enhanced by the adjunct administration of DCS at either the 4- or 8- week endpoints.
Conclusions: This controlled clinical trial failed to demonstrate an ability of DCS to boost the relapse prevention or treatment retention goals of CBT.
Financial Support: This project was supported by NIH grants R21DA025243 and F31DA025491 from the National Institutes of Drug Abuse.

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EFFECT OF SEX IN SELECTING BETWEEN FOOD AND COCAINE.

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Aims: Sex differences in cocaine dependence have indicated that women relative to men transition faster from first use to entering treatment. In animals, females rats show enhanced operant responding for cocaine relative to males. Furthermore, females in the estrus phase of their reproductive cycle display less avoidance of cocaine than males and nonestrus females as measured by the runway. We reasoned that sex differences would also be present when rats are given a choice between food and cocaine. To address this issue, we examined male, female, and OVX female rats during selection of food or cocaine.
Methods: On alternating days, rats were trained on a FI:20s schedule to respond on distinct levers for food or cocaine (0.4 or 1.0 mg/kg). After training, rats completed "choice tests" during which the rats could choose between the two reinforcers.
Results: During the low cocaine dose choice tests male rats showed a preference for food, however females were more likely to forgo food to select cocaine. Male and female rats both displayed increased cocaine choice at the high cocaine dose. Female rats earned more cocaine infusions than males and OVX females at both doses of cocaine, with OVX female rats being no different than male rats. However, there was no detectable impact of estrous cycle phase.
Conclusions: These data suggest that females are more sensitive than males to cocaine reinforcement, as they will sacrifice food for a low dose of cocaine and males will not. Moreover, these data suggest that females place a higher incentive value on cocaine relative to food than males regardless of cocaine dose, and that ovarian hormones are necessary for the expression of this behavior, but, unlike other measures of cocaine reinforcement, the choice to take cocaine and forgo other reinforcers is not linked to the reproductive cycle.
Financial Support: Supported by National Institute of Drug Abuse grants (1R01DA027525; 1R21DA027115) and a National Alliance for Research on Schizophrenia and Affective Disorders Young Investigator Award to TEK.

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TRAJECTORIES OF COCAINE AND BLOOD PRESSURE OVER 18 YEARS: THE CARDIA STUDY.

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Aims: Although cocaine acutely raises blood pressure, its long-term effects are unstudied. The Coronary Artery Risk Development in Young Adults study (CARDIA) allowed us to test if cocaine use trajectory was associated with blood pressure at 18 years, when use had diminished for most persons.
Methods: Past-month cocaine was queried at 3-5 year intervals among 4301 adults from 1987/88 (ages 20-32) to 2005/06 (38-50). They were sorted into cocaine trajectories with trajectory models. We compared trajectories for systolic and diastolic blood pressure (SBP & DBP) in 2005/06 (mmHg), and for categorical hypertension (BP>140/90 or receipt of medication) in 2005/06. Outcome comparisons excluded persons hypertensive at baseline. Generalized linear models adjusted for demographics, family history, physical & psychosocial characteristics, alcohol & tobacco.
Results: Three groups emerged: Nonusers (NON, 85%), Persistent Low Frequency Users (PLFU, 13%), and Early High Frequency Users (EHFU, 2.6%). In unadjusted analyses, DBP was higher among EHFU (75, SD 11), versus NU (72, SD 11) and PLFU (74, SD 11) ($p<.001$). Adjusting for covariates, this difference was unchanged with EHFU having DBP 3 mm Hg higher than NU ($p=0.03$). Systolic BP was also higher among EHFU (120, SD 16) in comparison to NU (115, SD 14), with PLFU in between (118, SD 14) ($p<.001$). This difference was not significant after multivariable adjustment ($p=0.08$). Additionally, trajectory groups did not differ in regard to categorical hypertension in 2005/06.
Conclusions: In a diverse community based cohort, a trajectory of elevated cocaine use before age 25 and some continuing use thereafter was associated with 3 mm Hg higher diastolic blood pressure. Categorical hypertension was not associated with cocaine trajectory. A 3-point difference in blood pressure is modest relative to cocaine's acute effects. However, it is comparable to differences seen in association with variations in diet and salt intake, and may hold health implications on a population basis.
Financial Support: NIDA R01-DA-025067; NHLBI N01-HC-95095

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LEARNING AND MEMORY DIFFERENCES IN THE DOPAMINE RECEPTOR D2 TAQ1A & C957T GENE SNP AMONG HIV-POSITIVE ALCOHOL ABUSERS.

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Aims: Despite Antiretroviral Therapy adherence, People Living With HIV (PLWH) show neurocognitive deficits (e.g. memory, learning), which are secondary to cerebral dopaminergic degeneration and which may promote "unnatural reward" seeking risky behaviors like hazardous drinking. Single Nucleotide Polymorphisms (SNP) of the ANKK1 gene (Taq1-A1 allele) and the C957T gene (T-allele) have been associated with alcoholism, which prompted this study of DRD2 allelic discrimination, neurocognition and alcohol use.
Methods: 28 males & 20 females alcohol abusing PLWH were classified as harmful, and hazardous drinkers (HD) (AUDIT score > 7) or non-HD. Neurocognition was assessed using the Auditory Verbal Learning Test (AVLT). Blood was drawn for allelic discrimination of ANKK1 (Taq1A) and C957T genes to assess their impact on alcohol behaviors and cognitive performance.
Results: Genotype frequencies for ANKK1 gene were A1+(46%), A1A2(40%), A2+(14%) and for C957T gene were TT(73%), CT(25%), CC(2%) with no significant age, gender, ethnic and racial differences. Noteworthy, a significant increased risk (AUDIT score > 17) was identified among participants having the haplotype A2 (RR=3.9 95% CI 1.4-10.7, $p=0.007$). HD tended to have lower learning rate (34.6±7.8 vs. 38±7), total learning scores (6.5±4.9 vs. 9.8±6.6), and proactive interference scores (1.08±0.071 vs. 1.48±0.141) $p=0.02$. Significant differences were found among the C957T genotypes in relation to AVLT corrected total learning score ($\chi2=79.25$, $p=0.001$), proactive interference score (T1/T6: $\chi2=56.7$, $p=0.026$) and delayed recall score (T8/T7: $\chi2=72.92$, $p=0.004$) .
Conclusions: Our results suggest that the ANKK1 gene, which presumably lowers DRD2 expression, is associated with alcohol dependence. Furthermore, results suggest that both hazardous alcohol drinking and C957T genotypes influence neurocognition.
Financial Support: Study Funding RO1AA017405.

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DOES MARIJUANA USE TRAJECTORY PREDICT SELF-REPORTED DEPRESSIVE SYMPTOMS AMONG COMMUNITY-BASED ADULTS FOLLOWED FOR 20 YEARS (THE CARDIA STUDY)?

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Aims: Depressive symptoms and marijuana use often co-occur. Prospective studies suggest marijuana use predicts adjustment problems and depression in young adulthood. Whether such associations are evident in middle age has not been assessed in prospective data.
Methods: Repeated measures of marijuana use were collected in the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a cohort of young adults balanced for race, gender, and education, recruited in 1985-6 (ages 18-30) and followed for 20 years. SAS PROC TRAJ was used to iterate marijuana use trajectories based on repeated queries of recent (last 30 days) marijuana use. We assessed whether different marijuana use trajectories were associated with depressive symptoms (>16 on the CES-D Scale) at year 20, controlling for age, race, sex, education, partnered status, economic difficulty, life stress, childhood environment and baseline depressive symptoms.
Results: Five marijuana trajectory groups emerged among 4803 participants: Non-Users (n=2935), Occasional Users (OU) (n=996), Persistent Users (PU) (n=202), Increasing Users (IU) (n=238) and Decreasing Users (DU) (n=432). Compared to Nonusers, three trajectory groups (Persistent, Increasing and Decreasing Users) had significantly higher mean CES-D scores and proportions of persons with CES-D>16 at four study examinations (from 1990/01 to 2005/06). Adjusting only for demographics and economic difficulty, the Odds Ratio (OR) for significant depressive symptoms remained elevated, compared to nonusers: for PU 2.1[95% CI, 1.3-3.3]; IU 1.8[1.2-2.7]; DU 1.8 [1.3-2.4]. However, these associations became non-significant after controlling for life stress, childhood environment and social support.
Conclusions: Marijuana drug use trajectory was not independently associated with later depressive symptoms among middle-aged adults.
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TREATMENT ENGAGEMENT AND RE-ENGAGEMENT STRATEGIES FOR SYRINGE EXCHANGERS.

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Aims: Most injection opioid users are not involved in substance abuse treatment. The damaging individual and public health consequences of this problem include the more likely transmission of HIV and other blood-borne diseases. Community syringe exchange programs (SEPs) typically engage severely impaired injection drug users, and provide ideal settings to evaluate strategies for improving treatment enrollment in this subgroup of injection drug users. We will present
12 month outcomes from a randomized clinical trial evaluating the efficacy of three different interventions to increase substance abuse treatment enrollment and re-enrollment in new SEP registrants in Baltimore, Maryland.
Methods: Opioid users enrolled in the Baltimore Needle Exchange Program (n = 281) were randomly assigned to one of three treatment referral conditions: 1) motivational enhancement therapy (MET); 2) motivational enhancement therapy plus modest incentive vouchers contingent on attending sessions and entering treatment (MET+I), or 3) standard SEP referral (SR). MET and MET+I subjects that enrolled in but subsequently left treatment were eligible to receive additional MET sessions to re-motivate treatment-seeking (MET+I subjects received vouchers for treatment re-engagement). Subjects were followed for 12-months.
Results: MET+I subjects had the highest rates of any treatment enrollment (MET+I: 52%; MET: 32%; SR: 35%; $x2 = 9.12$, $p = .01$) and methadone maintenance enrollment (MET+I: 40%; MET: 20%; SR: 16%; $x2 = 16.7$, $p < .001$) during the course of the intervention. Following the intervention phase, MET+I subjects were also more likely to re-enroll in treatment after discharge (MET+I: 64%; MET: 28%; SR: 37%; $x2 = 9.30$, $p = .01$).
Conclusions: Strategies that dynamically link SEPs with substance abuse treatment can improve the harm reduction benefits of both of these community-based interventions, especially when modest incentives for treatment seeking and re-engagement are provided.
Financial Support: This research was supported by NIDA Grant R01 DA12347-04 (M. Kidorf, P.I.)

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QUALITY VS. QUANTITY OF COPING SKILLS FOLLOWING COMPUTERIZED CBT.

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Aims: This study examined changes in the quality and quantity of coping skills acquired from a computerized cognitive behavioral therapy for substance use disorders program (CBT4CBT), and tested for the presence of mediation.
Methods: Data were gathered from a sample of 73 substance dependent individuals participating in a randomized controlled trial evaluating the effectiveness of CBT4CBT as an adjunct to treatment as usual (TAU) over an 8-week period. Participants completed an audio-taped role play assessment of coping skills at baseline, end of treatment, and again at a 3-month follow-up assessment. Independent evaluators rated participant responses according to the number of coping responses and the quality of coping responses provided. Repeated measures ANOVAs were used to evaluate changes in coping responses over time according to treatment condition, and mediation was tested using a series of linear regressions.
Results: Fifty-two participants (CBT4CBT=24; TAU=28) completed the coping skill assessment at baseline and end-of-treatment. No differences were found between groups on demographic variables or amount of substance use upon treatment entry. Participants assigned to CBT4CBT demonstrated a significantly greater increase in the quality of their overall coping responses, compared to those assigned to TAU ($F=6.77$, $p<.05$), and these differences remained significant 3 months after treatment completion. There were no changes over time in the number of coping responses provided by participants in either group. The quality of overall coping responses mediated the effect of treatment on participants' duration of abstinence during the follow-up period.
Conclusions: These findings suggest that assignment to the computerized CBT program improved the quality of participants' coping skills more than standard outpatient treatment. This is the first study to test and support quality of coping skills acquired as a mediator of the effect of CBT for substance use (Kiluk et al, in press).
Financial Support: This study was supported by the National Institute of Drug Abuse (NIDA) grants: R37-DA015969, K05-DA00457, P50-DA09241, and T32-DA007238.

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EXPANDING THE CONTINUUM OF CARE IN OPIOID AGONIST TREATMENT USING WEB-BASED VIDEOCONFERENCING.

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Aims: Web-based videoconferencing technologies hold the potential to improve delivery of evidence-based substance abuse interventions because they allow patients to access "real time" professional services from the convenience of their homes. These benefits may be especially important for patients in community-based opioid treatment programs (OTPs), who experience many obstacles to attendance of on-site counseling and are often poorly adherent. Reducing the inconvenience of attending counseling can improve rates of adherence and free up time for patients to pursue other activities essential to rehabilitation.
Methods: The present study evaluates the efficacy of using eGetgoingTM - a web-based videoconferencing platform- to deliver individual counseling using delivery schedules routinely employed in community-based OTPs. Participants at a community-based OTP with computer and Internet access (n = 80) are randomly assigned to receive weekly individual counseling onsite or via the eGetgoing platform for 3 months. Treatment satisfaction was measured with the Client Satisfaction Questionnaire and therapeutic alliance was measured with the Helping Alliance Questionnaire.
Results: 18 subjects have completed the study (eGetgoing=8; routine=10). Compared to baseline, rates of attendance to individual counseling sessions were similar for both the Routine, in-person group (baseline= 90%, study= 86%, p=ns) and the eGetgoing group (baseline= 82%, study= 81%, p=ns). CSQ scores were unchanged for both groups (routine pre-study=3.8, post-study=3.7, p=ns; eGetgoing pre-study=3.5, post-study=3.6, p=ns). HAQ scores remained high over the course of the study (Routine patient pre-study=5.5, post-study=5.6, p=ns; eGetgoing patient pre-study=5.3, post-study=5.4, p=ns). Similar results were obtained for the HAQ therapist assessment (Routine pre-study=5.0, post-study=5.1, p=ns; eGetgoing pre-study=4.8, post-study=5.0, p=ns).
Conclusions: Preliminary results indicate that web-based counseling services can be integrated into a community-based methadone treatment program without reducing patient satisfaction or treatment response.
Financial Support: NIH 1RC1DA028189

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PRENATAL STRESS AND GENETIC BACKGROUND INTERACT TO DETERMINE COCAINE-SEEKING BEHAVIOR IN MICE.

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Aims: Cocaine addiction is mediated by a complex phenotype resulting from gene-environment interactions. Although there is substantial support for both the role of genetic background and early environmental stress in determining addiction vulnerability, little research has addressed the potential interaction between these variables. Accordingly, we determined the effect of prenatal stress (PNS) in two genetically-distinct, inbred strains of mice (C57BL/6J and DBA/2J) on 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 with the other compartment. Then, each mouse was allowed to move freely between the two compartments to determine the relative preference for the cocaine-paired compartment (i.e. conditioned place preference).
Results: PNS significantly increased the magnitude of the CPP in B6, but not D, mice. Conversely, D2, relative to B6, mice exhibited increased cocaine-induced locomotion, greater sensitization of cocaine-induced locomotion, and increased conditioned locomotion, however, none of these locomotor measures were significantly impacted by PNS.
Conclusions: The results of the present study indicate that genetic background interacts with PNS to determine cocaine-seeking behavior in adult mice, thus, PNS and recombinant inbred mouse strains may offer an avenue to elucidate the details of the impact of gene-early environment interactions on adult drug-seeking and, potentially, addiction vulnerability.
Financial Support: Supported by National Alliance for Research on Schizophrenia and Affective Disorders Young Investigator Awards to TEK and KKS, NIDA (1DA027115-01) to TEK, and NIDA (1DA024038-01) to KKS.

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RANDOMIZED CONTROLLED TRIAL OF CRAFT VS. TREATMENT ENTRY TRAINING ALONE FOR FAMILY MEMBERS OF TREATMENT-RESISTANT INDIVIDUALS.

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Aims: We replicated previous work evaluating the efficacy of Community Reinforcement and Family Training (CRAFT) in promoting treatment entry of treatment-resistant individuals with drug use disorders (IDUDs) and asked whether the treatment entry training (TEnT) component of CRAFT was by itself sufficient to produce similar rates of treatment entry.
Methods: Concerned significant others (CSOs; N=115) of IDUDs were randomly assigned to receive: 1) the full CRAFT program (12 sessions), 2) TEnT only (6 sessions); or 3) Al-Anon Facilitation Training (AFT; 12 sessions), which introduced and engaged them in a widely available 12-Step program for CSOs. Treatment entry of the IDUDs was monitored up to 9 months after the CSO enrolled in the study.
Results: Compared to AFT, both CRAFT (OR = 2.7, 95% CI = 1.1 – 6.9) and TEnT (OR = 2.9, CI = 1.2 – 7.5) produced significantly higher rates of IDUD treatment entry, and CRAFT and TEnT did not differ from each other (OR = 1.1, CI = .4 - 2.7). TEnT produced higher rates of successful IDUD transfer to community-based treatment programs than AFT ($\chi 2$ = .045, OR = 3.22, CI = 1.2 - 8.6), however there was a trend for CRAFT participants attending more community treatment sessions than TEnT and TEnT participants attending more sessions than AFT.
Conclusions: TEnT by itself produces rates of IDUD treatment entry comparable to the full CRAFT program and can be accomplished in fewer sessions; however engagement in community-based treatment was low overall. Strategies to improve community treatment retention are needed and the full CRAFT program may be important in this respect. Additional studies are needed to examine this possibility.
Financial Support: This work was supported by a grant from the National Institute on Drug Abuse (R01 DA018696)

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CORRELATION BETWEEN ANTIRETROVIRAL THERAPY INITIATION DURING INCARCERATION AND ENROLLMENT IN OUTPATIENT HIV CARE AMONG NEWLY RELEASED INMATES IN ODESSA REGION, UKRAINE.

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Aims: In Ukraine HIV incidence in prisons is about 10 times higher than in general population. We aimed to investigate the proportion of newly released inmates who timely enroll in HIV outpatient care.
Methods: We conducted the retrospective cohort study of 354 HIV-infected inmates (including 38 persons receiving ART during incarceration), released from Odessa Male Correctional Colony #14 for Recidivists. The logistic regression analysis was used to examine the factors associated with the enrollment to HIV outpatient care within 60 days after release from prison and to calculate adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs).
Results: Among HIV-positive inmates released during January 2008 – August 2010, 91% reported the experience of injection drug use as the probable way of their HIV acquisition. Along with other factors, initiation of ART in prison was associated with successful post-release enrollment in HIV care. In the entire study group, 53 ex-inmates enrolled in AIDS Center within 60 days of release (14.9 %). However, the inmates who were on ART at the time of their release (N=38, or 10.7% of the cohort), had higher rates of enrollment in HIV out-patient care: 29 of them (76.3 %) timely registered in AIDS Center.
Conclusions: 1. Initiation of ART in prison can be a motivation factor associated with successful linkage to HIV care after release into community.
2. Large percent of HIV-positive inmates fail to go into HIV care after their release from prison. Effective discharge planning programs and more coordination between correction and HIV care institutions is needed to ensure HIV care among newly released inmates.
3. Correction system is an important place to initiate treatment of HIV infection, especially for individuals with drug addiction.
Financial Support: The Ministry of Health of Ukraine

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DEVIANT SOCIALIZATION MEDIATES TRANSMISSIBLE AND CONTEXTUAL RISK OF CANNABIS USE DISORDER DEVELOPMENT: A PROSPECTIVE STUDY.

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Aims: This study examines joint contribution of individual transmissible liability to addiction and contextual factors in the development of illegal drug use in adolescence and subsequently cannabis use disorder. It is hypothesized that the association of transmissible liability and parental involvement with cannabis use disorder between childhood and young adulthood is mediated by (1) performing household tasks as indicator of cooperative behavior in childhood; (2) normative attitudes and peer environment during adolescence and (3) consumption of illegal drugs in young adulthood
Methods: Two hundred fifty-four male children of substance use disorder (SUD+) and SUD- fathers participated in the study at ages 10-12, 16, 19 and 22. Path analysis with dichotomous outcome was conducted to model the trajectory to cannabis use disorder taking into account transmissible liability, parent-child relationship and cooperative behavior at baseline (age 10-12), normative attitudes and peer environment during mid-adolescence (age 16), use of illegal drugs in early adulthood (age 19), and cannabis use disorder (age 22).
Results: The results of path analysis confirmed the hypotheses that transmissible SUD liability and parental involvement are associated with performance of household tasks at age 10-12 which presages non-normative socialization at age 16, which, in turn, portends illegal drug use at age 19 and subsequently cannabis use disorder at age 22.
Conclusions: These findings indicate that cannabis use disorder is an outcome of deviant socialization originating in transmissible risk and adverse family context. Accordingly, promoting normative socialization may be an effective strategy for preventing cannabis use disorder.
Financial Support: This research was supported by Grants P50-DA005605, K02-DA017822.

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ACUTE AND RESIDUAL INTERACTIVE EFFECTS OF REPEATED ADMINISTRATION OF ORAL METHAMPHETAMINE AND ALCOHOL IN HUMANS.

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Aims: Although methamphetamine and alcohol are commonly used together in a binge-like pattern, empirical data investigating repeated effects of the combination are lacking. The current study examined acute and residual mood, performance, and physiological effects of methamphetamine alone, alcohol alone, and the combination.
Methods: Nine adult male volunteers completed this 20-day within-participant, residential laboratory study. During four 5-day blocks of sessions, participants were administered oral methamphetamine (0, 10 mg) combined with alcohol (0, 0.375, 0.75 g/kg) 3 times (Day 2: AM, Day 2: PM, and Day 3: PM). Breath alcohol concentrations, cardiovascular, subjective, and cognitive/psychomotor performance effects were assessed before drug administration and repeatedly thereafter. Subjective and objective sleep measures and residual effects were also assessed.
Results: Following initial drug administration, the methamphetamine-alcohol combination produced greater increases in heart rate and ratings of 'good drug effect' than either drug alone. Methamphetamine attenuated alcohol-related performance decrements and feelings of intoxication, whereas alcohol attenuated methamphetamine-related sleep disruptions. By the third administration, many effects significantly diminished, suggesting development of tolerance. Few residual effects were observed.
Conclusions: In conclusion, compared to either drug alone, methamphetamine combined with alcohol produced greater euphoria and fewer undesirable effects, which may explain frequent combinative use, while increased cardiovascular measures raises safety concerns.
Financial Support: Supported by DA03746 and DA023883.

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PAIN ACCEPTANCE AND SUBSTANCE USE SEVERITY IN ADDICTIONS TREATMENT PATIENTS WITH PAIN.

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Aims: In individuals with SUDs, greater pain severity is associated with higher levels of substance-related problems at treatment entry and poorer post-treatment substance-related outcomes. However, other factors related to the experience and management of pain, such as pain acceptance, have not been examined as correlates of greater substance use severity. This study utilized cross-sectional data from patients recruited from a large residential SUD treatment program with significant pain to examine the association between baseline pain acceptance and severity of substance-related problems.
Methods: A total of 351 adults receiving residential SUD treatment were assessed for their pain level, pain acceptance and pre-treatment substance use. The average age of the sample was 35.6 years (SD = 10.8). The sample was 76% male and 65% self-identified as white, 27% African American and 8% as another race. Over half (56%) of those entering treatment for SUDs reported moderate or greater pain. All subsequent analyses were based on these individuals.
Results: In adults seeking SUD treatment, greater pain acceptance was associated with a significant decrease in frequency of pre-treatment drug problems ($p < .05$) and prescription pain medication misuse ($p < .01$) after controlling for age, gender and race. Pain acceptance was not significantly associated with alcohol-related problems.
Conclusions: Pain is common in adults treated for substance use disorders. Greater acceptance, or a tendency to effectively cope with pain, was associated with decreased severity of drug and pain medication misuse. Other work has demonstrated that psychosocial behavioral interventions can significantly increase the use of effective acceptance-based strategies to address pain. The present findings suggest that these acceptance-based strategies may be important to test as a mechanism to decrease substance misuse in SUD patients with pain.
Financial Support: This project was supported with pilot funds from the Department of Psychiatry at the University of Michigan.

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SLEEP PROBLEMS AND SUICIDE ATTEMPTS IN ADULTS SEEKING ALCOHOL USE DISORDER TREATMENT IN POLAND.

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Aims: Worldwide, an estimated 900,000 adults die by suicide every year. In Poland, 4,384 people died by suicide in 2009. The risk of suicide is particularly high for individuals with alcohol use problems. Research on risk factors for suicide in those with alcohol use disorders is still preliminary. One risk factor in the general population is sleep problems. Given the association between sleep problems and alcohol use, it is possible that sleep problems may play a particularly important role in suicide risk among those with alcohol use disorders. For the present study, we hypothesized that self-report of sleep problems would be associated with greater likelihood of past suicide attempts in a sample of adults in alcohol use disorder treatment in Poland.
Methods: The sample included 154 patients consecutively admitted to addiction treatment programs in Warsaw, Poland, who met criteria for alcohol dependence. Participants completed a battery of self-administered and interview-based measures that included items related to demographic characteristics, alcohol use, sleep problems and prior suicidal behaviors. Multivariable logistic regression models were used to examine the association between insomnia and suicide attempt.
Results: In models that controlled for age, gender, and days of recent drinking, greater severity of sleep problems as measured by the Insomnia Severity Index (ISI) was associated with an increased likelihood of lifetime suicide attempt (OR = 1.05; 95% CI: 1.01, 1.10 per unit increase in the ISI).
Conclusions: In Polish adults treated for alcohol use disorders, more severe insomnia was associated with increased risk of prior suicide attempt. These results highlight the need to assess for sleep problems in alcohol treatment settings and to further examine the potential consequences of poor sleep in this population.
Financial Support: NIAAA and Fogarty International Center grant 5D43TW007569-05

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LEVELS OF KNOWLEDGE ABOUT THE RISKS AND SAFE USE OF OXYCONTIN® AMONG PRESCRIBERS OF OXYCONTIN®

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Aims: An FDA-required Risk Evaluation and Mitigation Strategy (REMS) for OxyContin (oxycodone HCL controlled-release) Tablets was launched that included distribution of a Healthcare Provider Training Guide to >164,000 OxyContin prescribers. The purpose of this survey was to measure the awareness and understanding of the risks and safe use of OxyContin among prescribers of OxyContin before the REMS was introduced.
Methods: A structured questionnaire for online administration was developed. The survey consisted of 14 multiple-choice questions with 27 correct response items and 26 incorrect items based on elements of risk and safe use described in the Training Guide. Those surveyed were randomly selected from a list of US OxyContin prescribers between October 2009 and March 2010.
Results: A total of 429 prescribers completed the survey. A high proportion (>85%) correctly identified 15 of the 27 correct responses, but 6 of 27 correct items were identified by <70% of prescribers. The lowest scores for correct response items were for "Concomitant use of OxyContin and cytochrome P450 3A4 inhibitors may possibly increase or prolong adverse effects leading to potentially fatal respiratory depression" (56% correct), and "Individuals who are considered at increased risk of OxyContin abuse include individuals with a personal or family history of mental illness such as major depression" (58% correct). Some prescribers erroneously identified incorrect response items as correct. For example, 33% thought that OxyContin is indicated for pain relief in the immediate postoperative period when the Training Guide states it is not, and 24% incorrectly responded that patients should be instructed to dispose of unused OxyContin in the trash when the Training Guide states it should be flushed down the toilet.
Conclusions: Pre-REMS gaps in prescriber knowledge about the risks and safe use of OxyContin were identifed. These results will help to target important areas for prescriber education about the safe use of OxyContin.
Financial Support: Authors are employees of Purdue Pharma L.P.

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CHILDREN'S EXPOSURE TO VIOLENCE IN SUBSTANCE-ABUSING HOMES.

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Aims: Children are disproportionately present in homes in which there is a police call for domestic violence. In these instances they are often exposed to parental substance use (e.g., Fantuzzo et al., 2007). The present study examined substance-abusing parents' reports of children's exposure to intimate partner violence (IPV) at the initial substance abuse treatment contact.
Methods: Intake sheets for a 12-month period (i.e., November 2008 – November 2009) were reviewed for individuals seeking treatment for substance abuse (89 males, 49 females) who were married/living with a partner and had children in the home. Drug of choice was equally divided between alcohol and other substance. On average, parents had 2 children in the home.
The partner initiating treatment completed items from the the CTS-2 assessing perpetration or victimization of various forms of IPV.
Results: Results revealed that 13% of respondents had been subject to or committed verbal aggression in the past year, 15% had pushed or shoved their partner or had been the victim of a push or shove in the past year, 7% had been kicked or kicked their partner in the past year, 12% had thrown something or had something thrown at them by a partner in the past year, and 4% had experienced a partner pulling their hair in the previous year.
Conclusions: Children living with substance-abusing parents are exposed to IPV at rates similar to that in the population. However, these were self-reports given by only the parent entering treatment at treatment contact. They indicate the importance of screening for IPV, obtaining both partners' reports, and that mental health provides should work with clients to explore IPV. These results also warrant attention of parent- and child-based approaches to support children in these homes to prevent or reduce the development of risks associated with living with a substance-abusing parent.
Financial Support: This work was supported by the National Institute of Drug Abuse (R01 DA024740).

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CONTINGENCY MANAGEMENT FOR SMOKING CESSATION: DO PRIZES HELP METHADONE PATIENTS QUIT?

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Aims: Over 80% of methadone-maintained opioid dependent patients smoke cigarettes and are therefore, as a group, at elevated risk for adverse health consequences. Prize-based contingency management (CM), a behavioral treatment for reducing smoking, can be easily applied among methadone patients because these patients must attend the clinic frequently. Two related pilot studies were conducted to examine the feasibility of prize-based CM for reducing smoking among methadone patients.
Methods: In both studies, urine cotinine and expired carbon monoxide (CO) levels were primary outcome variables measured across a 1-week baseline, 4-week treatment, and 2-week second baseline. We predicted that cigarette smoking would be significantly reduced during the CM phase compared with the baseline phases. Study 1 (n = 7) required each participant to achieve an absolute cotinine cutoff score indicative of smoking abstinence (<100ng/ml) to obtain reinforcement 3 days per week and low CO scores (<8ppm) two days per week. In contrast, Study 2 (n = 6) required gradual reductions in cotinine levels on a semi-quantitative scale to obtain reinforcement (i.e., shaping of abstinence) three days per week, and low CO scores on the other two days.
Results: Repeated measures analysis of variance revealed that participants in both studies significantly reduced their CO ($p < .001$) and cotinine ($p < .05$) levels during the treatment phase. One participant in Study 1 (14%) and half of the participants in Study 2 (50%) obtained CO and cotinine scores indicative of abstinence.
Conclusions: Overall, our findings provide initial evidence that prize-based CM may be an effective intervention for reducing cigarette smoking among methadone maintained outpatients and that a larger-scale investigation of the relative effectiveness of absolute abstinence and shaping is warranted.
Financial Support: NIH grant DA021839 and Joe Young, Sr. Funds (State of Michigan) supported this study.

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WHAT IS HAPPENING IN GROUP? CODED OBSERVATIONS OF TREATMENT-AS-USUAL IN OUTPATIENT GROUP COUNSELING.

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Aims: While group therapy remains the most common form of treatment for substance abuse disorders, little is known about the content employed or skill level community counselors possess to lead outpatient group sessions.
Methods: Within the context of an NIH-funded pre-post Relapse Prevention (RP)curriculum training study, we observed 4 baseline groups from 10 counselors recruited (client N = 132) from 4 outpatient treatment locations and live-coded each session for content and skill. We observed 2 groups on pre-selected RP topics (Coping with Craving and Drug Refusal Skills) and 2 on general topics, coding each for general skill and Frequency (1-7) and Skillfulness (1-7) on session-specific RP constructs. Counselors also documented the type of groups led and the topics covered in their general practice on a web-based calendar completed for 12 weeks.
Results: On average, counselors reported leading 6 groups per week with 10 clients per group. Fifty-six percent of reported groups involved teaching and processing recovery-oriented information: Coping Skills Training (21%), Anger Management (14%), Psychoeducation (13%), and 12 Step Principles (8%). Counselors generally demonstrated acceptable levels at Teaching (Freq. M = 4.1, SD = 0.91; Skill M = 3.3, SD = 0.41) and Processing group behaviors (Freq. M = 4.9, SD = 0.74; Skill M = 4.1, SD = 0.60), but very low levels of Eliciting Commitment from clients (Freq. M = 1.5, SD = 0.47; Skill M = 3.2, SD = 0.56). Seventy percent of counselors reported reading CBT or RP manuals in the last two years and 80% reported attending college courses on CBT or RP. However, baseline use of topic-specific RP behaviors in prompted groups was very low (Freq. M = 1.9, SD = 0.58), while Skillfulness was "adequate" (M = 3.6, SD = 0.72).
Conclusions: Counselors in community treatment programs would benefit from general training and supervision in core group-facilitation skills and in the use of evidence-based content.
Financial Support: NIDA: 1R01DA025034-01A1

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STATE POLICY AND AVAILABILITY OF MEDICATIONS IN SUBSTANCE ABUSE TREATMENT PROGRAMS.

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Aims: Despite the expanding number of medications for treating substance use disorders (SUDs), few publicly funded treatment programs have adopted them. This study aimed to examine the role of state policy in multivariate models of medication adoption.
Methods: Survey data were collected from 250 administrators of publicly funded treatment programs (86% response rate). Measures included adoption of any and number of SUD medications, program characteristics, and 4 perceptions of state policy: support of the Single State Agency (SSA) for medication-assisted treatment (MAT), knowledge of medications on the Medicaid formulary, ability to use state funds to buy medications, and ability to use state funds for physician time. Models were estimated using logistic and negative binomial regression.
Results: Only 33% of programs had adopted any medications, averaging 0.9 medications (SD = 1.6). At the bivariate level, all 4 state policy measures were associated with any adoption, and 3 were related to the number of medications. The odds of any SUD medication adoption and the number of medications were positively associated with perceived presence of medications on the Medicaid formulary, after controlling for program characteristics. SSA support for MAT was positively associated with the odds of any adoption. Other key covariates included ownership, accreditation, offering detoxification, providing both outpatient and inpatient/residential care, and number of physicians.
Conclusions: Medication adoption was greater in treatment programs aware of SUD medications being included on the state Medicaid formulary, but the perceived role of the SSA's support was limited to adoption of any SAT medications. However, nearly half of programs did not know whether medications were on the Medicaid formulary, suggesting that SSAs supportive of MAT may need to engage in greater dissemination of information about the Medicaid formulary to promote greater MAT adoption.
Financial Support: Supported by the Robert Wood Johnson Foundation Substance Abuse Policy Research Program (Grant 65111).

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GENDER DIFFERENCES IN NEURAL ACTIVITY DURING DRUG CRAVING AND GAMBLING URGES: AN FMRI STUDY.

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Aims: Urge or craving states are key features of cocaine dependence (CD) and pathological gambling (PG), are associated with severity of use, and predict relapse after treatment. Prior work has identified regional brain activations associated with urge states in PG and CD. However, such studies have used predominantly male samples, raising questions regarding the applicability of the findings to women with these disorders. Here we ask: Are there gender differences in the neural representation of craving between PGs and CDs? This question is crucial because gender differences in these populations have been consistently observed in both clinical and experimental contexts.
Methods: We used fMRI to examine neural activity in 110 participants (35 PG (13F), 30 CD (12F), and 45 healthy control (HC; 29F)) while they watched videos depicting cocaine use, gambling, and sad stories. Gender-by-Diagnostic-Group-by-Video ANOVAs were performed on neural activity during the initial and final periods of viewing.
Results: CDs reported drug craving when viewing cocaine videos and PGs reported gambling urges when viewing gambling videos. Group-by-Video interactions identified the subgenual ACC and dorsal ACC/mPFC during the initial and final periods, respectively, consistent with prior studies of male participants. A Gender-by-Group-by-Video interaction was found in mPFC, such that male but not female CD subjects showed increased activation to cocaine videos and female CDs or PGs showed decreased activation to sad videos. In both the posterior cingulate and insula/caudate, female but not male PGs showed increased activation to gambling videos and decreased activation to cocaine videos.
Conclusions: The findings illustrate both gender-independent and gender-specific patterns of neural responding associated with gambling urges and drug cravings in PG and CD. Gender differences in the neural substrates of each disorder highlight the need to develop gender-informed treatments.
Financial Support: NIDA R01-DA019039 and K12-DA00167; NIBIB R01-EB006494; NCRG Center-of-Excellence grant.

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GABA-B RECEPTOR POSITIVE MODULATORS: DIFFERENTIAL ENHANCEMENT OF THE DISCRIMINATIVE STIMULUS EFFECTS OF BACLOFEN AND GAMMA-HYDROXYBUTYRATE.

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Aims: CGP7930 and BHFF are positive GABA-B receptor modulators that enhance in vivo effects of the GABA-B receptor agonist baclofen, assessed by loss of righting in mice. The present study investigated their ability to enhance GABA-B receptor mediated discriminative stimulus effects in pigeons.
Methods: Eight pigeons were trained to discriminate 7.5 mg/kg baclofen from saline, and another eight were trained to discriminate 178 mg/kg GHB from saline, using methods detailed elsewhere (e.g., Koek et al., JPET 317:409, 2006). All drugs were administered i.m., except the GABA-B receptor modulators, which were given p.o.
Results: In baclofen-trained pigeons, CGP7930 and BHFF substituted partially for baclofen (i.e., 41 and 74% baclofen-appropriate responding after 178 and 320 mg/kg, respectively). CGP7930 (100 mg/kg) and BHFF (32 mg/kg) significantly shifted the dose-response curve of baclofen at least 3-fold to the left, in a greater-than-additive manner, and did not significantly shift the curve of GHB. In GHB-trained pigeons, CGP7930 and BHFF substituted partially for GHB (i.e., 15 and 49% after 320 and 178 mg/kg, respectively). BHFF (56 mg/kg), but not CGP7930 (178 mg/kg), shifted the dose-response curves of baclofen and GHB at most 2-fold to the left, in an additive manner.
Conclusions: The finding that CGP7930 and BHFF enhanced the discriminative stimulus effects of baclofen in a greater-than-additive manner is consistent with their in vitro characterization as positive GABA-B receptor modulators. In contrast, their interaction with GHB was modest and not greater than additive. This differential enhancement is further evidence that the mechanisms mediating the effects of baclofen and GHB are not identical. A better understanding of these different mechanisms, and their involvement in the therapeutic effects of GHB and baclofen, could lead to more effective medications.
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EMPLOYMENT-BASED REINFORCEMENT OF ADHERENCE TO DEPOT NALTREXONE TREATMENT IN UNEMPLOYED OPIATE-DEPENDENT ADULTS: 12-MONTH FOLLOW-UP.

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Aims: Naltrexone could be used to treat opiate dependence, but patients refuse to take it. Extended-release depot formulations might improve adherence, but long-term adherence rates to depot naltrexone are not known. This study determined long-term rates of adherence to depot naltrexone and whether employment-based reinforcement can improve adherence.
Methods: Opioid-dependent unemployed adults were inducted onto oral naltrexone and randomly assigned to the Contingency (n=18) or Prescription (n=17) group. Participants were offered six depot naltrexone injections and invited to work at the therapeutic workplace, a model employment-based intervention for drug addiction and unemployment, each weekday for 26 weeks where they earned stipends for participating in job skills training. Contingency participants were required to accept naltrexone injections to maintain workplace access. Prescription participants could work independent of whether they accepted injections. At the conclusion of the trial, participants were offered a prescription for oral naltrexone and contacted six months later for a follow-up assessment including a urine screening.
Results: Throughout the trial, contingency participants accepted more naltrexone injections (81%) than Prescription participants (42%), but no participants in either group reported taking naltrexone at the 12-month follow-up. The groups provided similar percentages of urine samples negative for opiates and cocaine during the trial and at follow-up. Across groups, rates of opiate negative urine samples at the 12-month follow-up were similar to those during the trial, while rates of cocaine negative urine samples were marginally higher at the follow-up.
Conclusions: Employment-based reinforcement may be needed to maintain long-term adherence to naltrexone treatment.
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RISK-TAKING AND IMPULSIVITY IN METHAMPHETAMINE-DEPENDENT AND HEALTHY CONTROL PARTICIPANTS.

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Aims: We examined multiple phenotypes of impulse control and their influences on risk-taking behavior, using the Balloon Analogue Risk Task (BART; Lejuez, 2002).
Methods: Propensity for risk-taking was assessed using the BART; and impulsivity was measured by self-reports on the Barratt Impulsiveness scale (BIS), and Dickman Functional Impulsivity Inventory (DFII) and by performance on the Delay Discounting Task (DDT) in healthy control and in methamphetamine-dependent participants (HC; n=11 and MA; n=11). On the BART, a participant chooses to inflate ("pump") a virtual balloon to increase potential monetary rewards, or to cash-out and keep the reward at any point. Each pump carries a risk that the balloon will explode, resulting in loss of the entire reward. Either excessive or insufficient pumping represents suboptimal performance.
Results: Neither group exhibited optimal risk-taking. In both groups, steeper discounting in the DDT was associated with lower mean adjusted pumps (HC: R= -.596,p=.034, MA: R= -.507,p = .056). BIS scores were not correlated with mean adjusted pumps in either group, nor were number of adjusted pumps or cash outs correlated with any of the three measures of impulsivity in HC subjects. In the MA group, DFII scores were negatively correlated with mean adjusted pumps (R=-.758, p=.006) and positively correlated with number of cash-outs (R=.766, p=.003). Number of cash-outs also was correlated positively with DDT K scores in MA subjects (R=.632, p=.019).
Conclusions: It has been reported that HC individuals are risk-averse and exhibit greater sensitivity to losses than to rewards (Trepel, 2005). Data presented here suggest that the lack of risk-taking in MA individuals is not driven by risk aversion but the propensity to take immediate rewards rather than a potentially larger, later reward.
Financial Support: NIH grants R01 DA020726, R01 DA015179 (EDL), T90-DA022768, M01 RR00865 (UCLA GCRC), endowments from Pike Chair in Addiction Studies and the Green Family Trust (EDL).

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SMOKING REINFORCEMENT IS ASSOCIATED WITH INHIBITORY CONTROL PERFORMANCE IN ADULT REGULAR SMOKERS.

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Aims: Inhibitory control has been associated with a range of smoking outcomes and may increase risk for relapse during a quit attempt. The goal of this ongoing study was to evaluate the association between inhibitory control performance and smoking reinforcement.
Methods: Thirty-one regular smokers (15 females, 16 males; mean age = 34 years) who smoked at least 10 cigarettes/day were enrolled in a laboratory study of smoking reinforcement. Following screening and baseline sessions, participants completed 2 laboratory sessions: 1 following biochemically verified 24-hour smoking abstinence and 1 following smoking as usual conditions. During both sessions, participants completed a 90 minute Progressive Ratio (PR) task wherein the opportunity to smoke standardized puffs of a cigarette was available following a progressively greater number of button presses. A fixed amount of cash ($0.50) was available under a concurrently operating schedule. A continuous performance task (CPT) was also administered prior to the PR task in both sessions and commission errors were assessed as a measure of inhibitory control. Mixed model ANOVA was conducted to assess the effects of session on commission errors and linear regression was conducted to assess the influence of commission errors on the number of ratios completed for cigarette puffs.
Results: There was a significant main effect of condition on commission errors ($F = 6.36$, $df = 1$, $p = 0.02$) in that the abstinent day resulted in significantly more commission errors. Regression analyses revealed that commission errors significantly predicted the number of ratios completed for cigarette puffs (beta = 0.05, $p < 0.05$).
Conclusions: Results suggest that smoking abstinence significantly disrupts inhibitory control, which in turn increases the relative reinforcing effects of cigarette smoking. These findings suggest a putative behavioral mechanism by which abstinence induced inhibitory control disruptions may lead to increased risk for smoking relapse. Data collection for this study is ongoing.
Financial Support: This work was funded by NIDA grant 1R01DA025653 (PI: Kollins)

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PSYCHOMETRIC PROPERTIES OF CLINICAL MONITORING ITEMS.

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Aims: Monitoring the clinical status of substance abusing clients during treatment is recommended for decision making, quality improvement and reporting at both the case and program level. An outcomes monitoring system (OMS) requires an item set with face validity that assesses multidimensional clinical status, risk and protective factors for relapse/dropout, and treatment services; the items must also have adequate psychometric properties. Preliminary data on the response characteristics, sensitivity to change, test-retest reliability, and validity of items within a clinical OMS for outpatient treatment are reported.
Methods: Clients (n=133) in 2 outpatient clinics completed a series of weekly, self-administered, web-based assessments consisting of 29 clinical monitoring items for a 1 month period during treatment. Item responses were frequency counts of behaviors over the past 7 days, Likert-scales, or dichotomous ('Yes/No'). Responses were available to the client's counselor. A 2-day retest was completed for one assessment where the responses were not available to clinicians.
Results: Baseline item characteristics revealed variability in responses. Many items were skewed, e.g., for 7 items the same response option was selected by ≥80% of the sample. There were virtually no skipped questions (<1%). Sensitivity to change between the 1st and 2nd weekly administration of the item set revealed significant differences on 5 items, however, exact agreement ranged from 36 to 96% with the majority of items demonstrating <70% agreement. Test-retest exact agreement ranged from 54 to 100% with nearly ⅓ achieving >90% agreement, responses differed significantly on only 3 items; in all cases, more problems were reported when data were available to the clinician. Predictive validity for a baseline 9-item 'core' revealed 80% sensitivity and 60% specificity for treatment retention 30 days later.
Conclusions: Preliminary psychometric properties of a variety of monitoring items support their use in a clinical OMS.
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IMPULSIVITY AND SYMPTOMS OF ADHD AND ODD/CD IN DAILY-SMOKING ADOLESCENTS.

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Aims: Several studies have found a relationship between cigarette smoking and symptoms of attention-deficit hyperactivity disorder (ADHD) in the presence of co-occurring symptoms of oppositional (ODD) and conduct disorder (CD) in adolescents. Impulsivity is a core feature of externalizing behaviors including addictive behaviors such as cigarette smoking. In order to elucidate the association between impulsivity and symptoms of ADHD and ODD/CD in smoking adolescents, we analyzed the baseline data of adolescents participating in a smoking cessation program.
Methods: 40 (girls: n = 22) high school-aged, daily-smoking adolescents who reported smoking at least 5 cigarettes per day for the past 6 months and who had complete data were included in the analyses. Impulsivity measures are: (1) Barratt impulsiveness scale-II (BIS-II), a self-report measure of total trait impulsivity, non-planning, cognitive, and motor impulsivity; (2) Experiential discounting task (EDT), a computerized task assessing real-time delayed discounting; (3) Conners' continuous performance test-II (CPT), a computerized task that assesses inattention. A structured interview using the Youth Diagnostic Predictive Scales (DPS v. 4.32) assessed ADHD and ODD/CD symptoms. In the multiple regression analysis, ADHD and ODD/CD symptoms were the independent variables and each of the impulsivity subscales were the dependent variables.
Results: The results showed that ADHD symptoms but not ODD/CD symptoms, were associated with cognitive impulsivity on the BIS-II ($\beta = .37$, $p = .02$), higher hit rate standard error ($\beta = .36$, $p = .03$) and perseveration ($\beta = .47$, $p < .01$) on the CPT. ODD/CD symptoms but not ADHD were associated with greater impulsivity on delayed discounting, (EDT: $\beta = -.40$, $p = .02$).
Conclusions: The findings of this research indicate that aspects of impulsivity are differentially associated with ADHD and ODD/CD symptoms in daily smoking adolescents, and this information may be useful in developing a personalized smoking cessation intervention.
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RETENTION TO TREATMENT IN INCARCERATED AMPHETAMINE-DEPENDENT MEN WITH ADHD.

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Aims: The aim of the study was to investigate if severity of addiction and/or psychiatric co-morbidity predict drop out from treatment in amphetamine dependent men with co-morbid ADHD.
Methods: Fifty four incarcerated men who met the DSM-IV criteria for amphetamine dependence and ADHD were assessed for substance use and psychiatric co-morbidity using in Addiction Severity Index (ASI) and Structured Clinical Interview for DSM-IV diagnosis (SCID I, II). Composite scores were calculated for seven ASI subscales: Health, Drugs, Family and Social status, Legal status, Employment status and Psychiatric health. Background data for number of convictions and total time of incarceration was retrieved from criminal records. The population was divided into two groups, those who completed the 24 weeks of trial and those who dropped out before week 24.
Results: The mean age was 42.3 years (SD 10.5). All participants had an i.v. amphetamine use, the mean debut age was 18 years and mean length of use was 19, 6 years (SD 11). The participants had been incarcerated on average at 11.3 occasions (SD 8.2) The most frequent axis-II diagnoses were antisocial (50%), obsessive-compulsive (23%) and borderline personality disorder (18%) and prior alcohol dependence (44%), other substance use disorders and anxiety disorder (19%) were the most frequent axis-I diagnoses.
No significant difference was found in ASI composite scores or in psychiatric co-morbidity between those who completed the trial compared to those who did not.
Conclusions: The severity of addiction measured with ASI composite scores and the psychiatric co-morbidity did not affect the attrition to treatment.
Financial Support: The study was financially supported by Stockholm County Council and The National Board of Health and Welfare in Sweden

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HIV RISK BEHAVIORS AND INTERVENTION EFFICACY IN DRUG ABUSE TREATMENT TRIALS.

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Aims: Drug use and HIV risk behaviors are intertwined and predictive of one another. We sought to examine whether baseline HIV risk behaviors (injection drug use and risky sexual behavior) were related to drug use during follow-up; and whether intervention efficacy depended on HIV risk behaviors.
Methods: Six trials from the NIDA Clinical Trials Network were included. Baseline HIV measures included needle use, sharing needles, sharing dirty needles, condom use, and multiple partners in the last month. We defined drug use during follow-up based on percent negative urine drug screens (UDS).
Results: Overall, 348/1560 (22.3%) reported any needle use, and 80 (5.1%) reported needle sharing. 163 (10.4%) reported multiple partners. 747 (47.9%) reported sex without a condom, dropping to 106 (6.8%) when considering only those who were unmarried or reported multiple partners. Neither condom use nor multiple partners were associated with drug use during follow-up. However, 87.1% of those using dirty needles, vs. 81.6% of those using clean needles, and 52.1% of those not using needles, failed half or more of follow-up UDS ($p<0.0001$). Intervention efficacy depended on condom use (interaction $p<0.05$): among those reporting sex without condoms, 62.0% vs. 54.1% in intervention vs. control failed at least half of follow-up UDS ($p=0.03$). In the safe sex group, results were 57.2% vs. 59.6% ($p=0.52$). No interactions were observed for multiple partners, or for injection drug use measures.
Conclusions: Drug use treatment efficacy may be improved by considering other behavioral risk factors. Our finding of an interaction between condom use and intervention assignment in predicting drug use during follow-up bears further study. Our next steps will be to evaluate these relationships in the context of other clinical, demographic, and behavioral data, and to evaluate other follow-up measures to allow a more comprehensive understanding of drug use trajectories related to these risk behaviors.
Financial Support: U10DA013727

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UNHEALTHY ALCOHOL AND ILLICIT DRUG USE ARE ASSOCIATED WITH DECREASED QUALITY OF HIV CARE.

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Aims: To assess the impact of unhealthy alcohol and illicit drug use on the quality of HIV care. We hypothesized that quality of care would be lower among HIV-infected patients with unhealthy alcohol and illicit drug use.
Methods: We surveyed HIV-infected veterans enrolled in the Veteran's Aging Cohort Study about substance use and abstracted 5 HIV quality indicators (QIs) from medical records in the 12 months prior to enrollment: receipt of highly active antiretroviral therapy, *Pneumocystis jirovecii* pneumonia prophylaxis, *Mycobacterium avium* complex prophylaxis, ≥ 2 CD4 counts performed, and ≥ 2 HIV clinic visits attended, as indicated. Independent variables were unhealthy alcohol use (AUDIT-C score ≥4) and illicit drug use (self-report of stimulants, opioids, or injection drug use in past year). Main outcome was receipt of ≥ 80% of QIs. We estimated associations between substance use and quality of care using univariate and multivariable logistic regression, adjusting for age, gender, and race.
Results: The majority of the 3,410 patients were male (97%) and African-American (67%) with mean age of 49.1 years (SD 8.8). Overall, 26% had an AUDIT-C score ≥4, 22% reported illicit drug use in past year, and 72% received at least 80% of indicated QIs. The percentage of patients receiving at least 80% of QI's was lower for those with unhealthy alcohol use vs. not (65% vs. 74%, $p<.001$) and those using illicit drugs vs. not (65% vs. 74%, $p<.001$). After adjusting for age, gender, and race, unhealthy alcohol use (adjusted odds ratio [aOR] 0.71, 95% confidence interval [CI] 0.60, 0.85) and illicit drug use (aOR 0.73, 95% CI 0.62, 0.87) remained inversely associated with receipt of ≥ 80% of QI's.
Conclusions: Though the overall quality of HIV care for this cohort of HIV-infected patients was high, gaps in quality of care persist for those with unhealthy alcohol and illicit drug use. Interventions that address alcohol and illicit drug use in HIV-infected patients may improve the quality of HIV care.
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LITTER GENDER COMPOSITION ALTERS MATERNAL BEHAVIOR IN RATS.

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Aims: Responses to drugs and stress have common neural underpinnings and show sex differences. Previous work demonstrates that stress responsivity links to maternal care received; adult rats that received more anogenital licking and arched-back nursing show less stress responsivity than rats that received less of these as pups. However, these studies were performed in male rats only. There are sex differences in responses to stress and drugs that may reflect maternal care received. We tested if sex differences in maternal care could be manipulated by altering the gender composition of the litter hypothesizing that the dam would treat female pups in all female litters like male pups and less like female pups from mixed-sex litters. Further, because recent data suggest that polymorphisms in the OPRM1 gene of primates are associated with attachment we plan to examine DNA methylation levels of this gene in the offspring of these litters.
Methods: Litter gender composition (LGC) of rats was altered; litters were culled to 8 all male, all female, or half male/half female pups on postnatal (PN) day 1. On PN4, PN7, and PN10, the dam was placed in a test cage for 30-min. A pup was placed in the test cage for a 10-min videorecorded observation period. Frequencies of pup-directed (e.g., blanket nursing) and self-directed behaviors (e.g., self-grooming) were determined as well as times spent licking the anogenital region and the rest of the body of the pup.
Results: Body weight increased across days and on PN10, single-sex litters weighed more ($P<0.01$), an effect that was greater for male pups ($P<0.001$). Blanket nursing, which correlates inversely with arched-back nursing, was greater in mixed female litters and increased over days in single female litters ($P<0.05$). Times spent in anogenital licking were greater for male vs. female pups and for single vs mixed male litters (P's <0.05). Male pups also tended to receive more other body licking compared to female pups ($P<0.10$).
Conclusions: Results confirm that male pups received greater maternal care than female pups. We also show that LGC can alter the sex dependency of maternal care received.
Financial Support: DA-020117

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METHAMPHETAMINE-INDUCED CEREBRAL BLOOD FLOW CHANGES AND ITS IMPLICATIONS AS A RISK FOR PARKINSON'S DISEASE.

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Aims: Methamphetamine (meth) is a psychostimulant shown to induce neurotoxicity. Proposed mechanisms of meth-neurotoxicity include dopamine-quinone and reactive oxygen species aided neuroinflammation, blood-brain barrier dysfunction, and hyperthermia (review:Yamamoto et al,2010). We pose a new mechanism based on our findings of meth-induced vasoconstriction in select brain regions. AIM:To evaluate alterations in regional cerebral blood flow (rCBF) due to meth treatment.
Methods: Rats were administered an i.p. injection of 0.9% saline, 3mg/kg, or 9mg/kg meth. All treatment groups were perfused with FITC-LA at 2 or 24 hours post-injection. Chronic self-administering rats were also perfused to evaluate rCBF with chronic meth use. After perfusion, brains were prepared for fluorescence imaging.
Results: There was a distinct void of FITC-LA in the dorsal striatum (dStr) of rats administered 3 and 9mg/kg meth. In contrast, adjacent cortical and ventral striatal regions showed normal vasculature. The chronic treatment group also showed vasoconstriction in the dStr with nearby brain regions displaying normal vasculature.
Conclusions: Our data indicates that while the cortex and dStr are both supplied by the middle cerebral artery, only striatum undergoes reduced rCBF with meth treatment. Our findings and several clinical studies show that reduced rCBF is selective to sensorimotor regions of the striatum, while associative and limbic regions maintain normal rCBF(Chung et al,2010;Iyo et al,2006). Selective reduced rCBF may destroy dopamine (DA) terminals in the striatal region most affected by Parkinson's disease (PD). Recent clinical data suggest that meth-neurotoxicity can lead to increased risk for PD development in meth abusers (Callaghan et al,2010). Our study represents the first pre-clinical model of meth-induced reduced CBF to the dStr, a new mechanism of neurotoxicity. Exploration of this novel mechanism may provide an animal model for meth-induced PD risk and offer insight into how DA neuron loss occurs in idiopathic PD.
Financial Support: Supported by: Rush University

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BRAIN-REGION SPECIFIC CHANGES IN SEROTONIN 2C RECEPTOR AND PHOSPHOLIPASE D SIGNALING TRACK WITH A DISTINCT BEHAVIORAL PHENOTYPE EXPRESSED IN CONDITIONED HYPERACTIVITY TO COCAINE.

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Aims: Environmental cues can become classically conditioned to cocaine exposure and contribute to craving and relapse in addicts. Signaling through 5-HT2CR is implicated in the mechanisms underlying cocaine-associated conditioning events, including reward salience. We propose that 5-HT2CR signaling results in a downstream activation of PLD and hypothesized the dynamics in PLD and 5-HT2CR expression in amygdala, hippocampus or prefrontal cortex (PFC) may track with cocaine-cue dependent behavior during withdrawal.
Methods: Male rats received repeated pairings of a distinct test setting with saline or cocaine for 7 days. Paired and unpaired rats received cocaine (15 mg/kg, i.p.) in the activity monitor with motility assessment and home cage, respectively, and saline in the alternative setting; control rats received saline in both settings. A 30-min drug-free test for motility occurred 14 days after the last pairing; rats were sacrificed and brain tissue processed for Western analysis.
Results: Expression of conditioned hyperactivity was seen only in paired rats (843±39 counts/30min) vs. unpaired (699±43) or control rats (604±36; $p<0.05$). As hypothesized, we observed a concomitant increase in the synaptosomal membrane expression of both PLD (PLD1, PLD2) and 5-HT2CR in amygdala ($p<0.05$), while both were decreased in hippocampus ($p<0.05$) and did not differ in PFC (ns) of paired vs. unpaired and control groups.
Conclusions: The present findings suggest that the mechanisms via the 5-HT2CR-PLD mediated signaling in the amygdala and the hippocampus contribute to the salience of the drug-association with the environment. Elucidating the differential attributes of 5-HT2CR-PLD mediated signaling will be the invaluable first step to identify potential therapeutic targets of cue-based neuroplasticity underlying craving and relapse.
Financial Support: DA020087, DA024157, DA006511, Jeane B. Kempner Scholarship, Center for Addiction Research Pilot Funds

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DEVELOPMENT OF A NOVEL HIGH SCHOOL BASED INTERVENTION TO MOTIVATE A TOBACCO-FREE LIFESTYLE.

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Aims: Behavioral reinforcement programs that provide incentives for maintaining abstinence from cigarettes have been shown to be effective at motivating changes in smoking behaviors in adults and adolescents. We have developed and are in the process of evaluating a novel incentive-based intervention to motivate all students in a high school to adopt a tobacco-free lifestyle.
Methods: The intervention was implemented in two high schools, one in Connecticut and one in upstate New York. Focus groups of students (male and female, smokers and nonsmokers) and school officials were conducted within each school before and after a pilot period of program implementation, to help develop and refine the intervention and its execution. All students (smokers and nonsmokers) were encouraged to enroll in the program and pledge to be tobacco free for the rest of the school year. Enrollees were entered into weekly drawings for gift cards, which were provided only if the winners had not smoked and were biochemically confirmed to be tobacco free. Periodic special events were held to reinforce the tobacco free message, to recruit students to join the program, and to offer additional incentives for participation.
Results: The main endpoints for this study are enrollment into the program and changes in smoking behaviors assessed using pre- and post-intervention surveys. Overall, the intervention was well accepted by both students and faculty, with 69% of students in the NY high school and 71% of students in the CT high school enrolled into the program. Results from ongoing analyses examining survey and focus group evidence on changes in susceptibility to smoke, smoking behaviors as well as student and administrator reactions to the novel program will be presented.
Conclusions: This evidence suggests that incentive based programs to encourage tobacco-free lifestyles can be developed and implemented within school settings.
Financial Support: Supported by R01DA026450

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IMPLEMENTATION OF AN ELECTRONIC INFORMATION SYSTEM TO ENHANCE PRACTICE AT AN OPIOID TREATMENT PROGRAM: STUDY DESIGN & PRELIMINARY ASSESSMENT OF QUALITY AND RISK MANAGEMENT.

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Aims: The Addiction Research and Treatment Corporation, an outpatient opioid treatment program providing primary medical care for approximately 3,000 predominantly minority adults in New York City implemented an electronic health information system integrating counseling, social services, medical services, case management, HIV services, dispensing, and administrative/fiscal data. We combined our dispensing and social services program with eClinicalWorks, which became available through a grant obtained by the NYC Department of Health and Mental Hygiene. System performance was studied.
Methods: Five domains (Quality, Risks, Productivity, Satisfaction, Financial Performance) were chosen for evaluation utilizing a pre and post-implementation research design.
Results: Pre-implementation data have been collected and analyzed for all 5 domains. For Quality, annual medical assessments were timely for 82% of cases; and annual multidiscipline assessments were timely 72% of cases. For Risk, the number of measurable events totaled 87. Preliminary post-implementation data is available for 2 of the domains, Quality and Risk. For Quality, timeliness of annual medical and annual multidiscipline assessments was 92% and 93%, respectively, a highly statistically significant improvement. For Risk, the number of events was too small to provide meaningful pre-post comparison. Additional post-implementation data is being compiled.
Conclusions: The preliminary data showing highly significant improvement post performance for annual medical and multidiscipline assessments suggest that other measures of the electronic information system will show a positive trend.
Financial Support: National Institute on Drug Abuse (R01 DA022030)

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SOURCES OF DIVERTED PRESCRIPTION OPIOIDS AMONG A DIVERSE SAMPLE OF ABUSERS IN SOUTH FLORIDA.

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Aims: Accessibility of prescription opioids to non-patients is the result of their unlawful channeling from legal sources to the illicit marketplace (diversion). Empirical data on diversion remain absent from the literature. We examined sources of diverted opioids reported by participants in a South Florida study targeting diverse populations of opioid abusers (N=782). Sources of diverted medications were hypothesized to differ according to abusers' health insurance and physical health status, drug dependence, IDU, and primary opioid of abuse.
Methods: Eligible respondents were 18 years of age or older and reported misuse of a prescription drug 5 or more times in the past 90 days. Those who reported a prescription opioid (hydrocodone, IR oxycodone, ER oxycodone, methadone, morphine, hydromorphone or fentanyl) as their most frequently misused drug were included in the analyses. The highest potency opioids (hydromorphone, morphine and fentanyl) were rarely reported and were combined into a single category. Trained interviewers administered standardized health and social risk assessments, including detailed drug use histories and sources of abused prescription medications. Bivariate logistic regression models were developed to predict use of each diversion source by demographics and by the hypothesized independent variables.
Results: The most common sources of diverted medications were dealers, sharing/trading, legitimate medical practice (e.g., unknowing medical providers), illegitimate medical practice (e.g., pill mills), and theft, in that order. Sources varied by users' age, ethnicity, health insurance status, physical health status (including pain), drug dependence, IDU, and primary opioid of abuse.
Conclusions: Individual and health factors, as well as the potency of the abuser's preferred drug, appear to impact the choice of drug sources. Implications for prescription drug control policy are discussed.
Financial Support: This research was supported by NIH Grant R01DA021330.

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A CLINICAL TRIAL OF N-ACETYLCYSTEINE FOR COCAINE DEPENDENCE.

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Aims: The aim of the present study was to examine the extent to which N-Acetylcysteine (NAC) reduces cocaine use in cocaine-dependent individuals.
Methods: Participants were 122 cocaine-dependent individuals (66 African American, 92 Male) recruited for an 8-week double blind, placebo controlled trial of N-Acetylcysteine (NAC). Participants were randomized to receive placebo or one of two doses of NAC, 1200mg (600mg b.i.d.) or 2400mg (1200mg b.i.d.). Urine samples were collected at each research visit (1-3/week) and analyzed for quantitative levels of benzoylecognine. Medication compliance was assessed weekly by analyzing urine levels of riboflavin, which was incorprated into medication capsules(>1500 ng/ml considered compliant).
Results: Data were analyzed using the GEE approach, with 2 between-subjects factors: Baseline Use 30 days prior to the trial (>=11 or <11) and Medication Condition. Treatment Week served as a within-subjects repeated factor. Mean weekly level of log transformed benzoylecognine levels served as the dependent variable. The Intent to Treat (ITT) analysis (n=122) revealed a significant Baseline Use x Medication Condition x Treatment Week interaction, but post hoc analyses did not reveal group differences at any week. A follow-up analysis used a subset (n=94) of the ITT sample that eliminated outlier participants (i.e. negative UDS at baseline and throughout the 8 week trial) and included participants who demonstrated at least one week of riboflavin compliance. The 3-way interaction remained significant and post hoc data revealed that those receiving 1200mg NAC who also used <11 days prior to the study showed reduced bezoylecognine levels relative to their counterparts receiving placebo or 2400mg NAC at weeks 4 and 7.
Conclusions: Some beneficial effect of NAC was noted, as indicated by lower weekly log mean benzoylecognine levels, but only at the 1200mg dose, and only in those who were using cocaine less frequently prior to the start of the trial.
Financial Support: Grant support provided by NIDA DA019903.

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

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Aims: This study presents the first national prevalence estimates for drug-involved driving derived from the recently completed 2007 U.S. National Roadside Survey (NRS). The NRS involved randomly stopping drivers at 300 locations across the 48 contiguous states in the United States. Data were collected during four 2-hour night-time periods (Fridays and Saturdays) and one 2-hour day-time period at 60 sites. New to the 2007 NRS was the collection of additional types of biological samples (oral fluid and blood) to determine the presence of drugs other than alcohol in the driving population. We collected 7,719 oral fluid samples and 3,276 blood samples from drivers.
Methods: Oral fluid and blood samples were collected from survey participants and were analyzed using ELISA screening, followed by a confirmatory analysis by LC/MS-MS or GC/MS. Analyses of the oral fluid and blood samples were conducted to identify the presence of some 75 drugs and metabolites, including illegal, prescription, and over-the-counter drugs.
Results: Comparison of overall drug prevalence by time of day indicates that 11% of drivers in the day-time sample were drug-positive in oral fluid. This level was significantly lower than the 14.4% of night-time drivers who tested positive for drugs ($p < .01$). The most frequently encountered individual drug, other than alcohol, was marijuana. Comparison of drug categories by time of day revealed that, based on oral fluid analyses, almost 6% of day-time drivers tested positive for drugs in the "Illegal" category, as opposed to more than 10% of night-time drivers. There was a statistically significant difference between day-time and night-time drivers ($p < .01$).
Conclusions: The extent of drug use by weekend drivers is substantial, but the extent to which prevalence is related to crash risk has not been determined. That is the subject of a follow-on study involving 2,500 crash-involved drivers currently underway.
Financial Support: NHTSA, NIAAA, NIDA

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GESTATIONAL INTRAVENOUS NICOTINE INCREASES MOTIVATION FOR SUCROSE REWARD IN ADULT RAT OFFSPRING.

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Aims: Prenatal tobacco smoke exposure is correlated with low birth weight, sudden infant death syndrome, ADHD, cognitive and behavioral deficits as well as increased likelihood of drug abuse in human offspring. The purpose of the present study was to determine if intermittent, low-dose, IV nicotine exposure during gestation would alter motivation for sucrose reward in adult, rat offspring.
Methods: Pregnant dams were injected (3x/day) with 0.05 mg/kg nicotine or saline via internalized jugular catheters on gestational days 8-21. Beginning on post-natal day 70 both male and female adult offspring were trained to respond for a 26% (w/v) sucrose solution. After stable responding on a fixed-ratio (FR)-3 schedule for 26% sucrose was achieved, animals were tested for responding on varying sucrose concentrations (0, 3, 10, 30, and 56%) on an FR-3 schedule. Following FR-3 testing, animals responded on a progressive-ratio (PR) schedule for the same concentrations. All concentrations were presented according to a Latin square design during both FR and PR responding sessions.
Results: A mixed-design ANOVA conducted on the FR responding data indicated a main effect of sucrose concentration [$F(4, 92) = 38.792$, $P < .001$]. No other significant effects were detected between gestational nicotine (GN) and gestational saline (GS) animals on the FR data. Analysis of the PR responding data revealed main effects of sucrose concentration [$F(4, 104) = 23.733$, $P < .001$] and gestational treatment [$F(1, 26) = 5.500$, $P < .05$]. These results indicate that GN animals displayed higher rates of responding on the PR schedule, indicating that IV GN increases the motivation for sucrose reward.
Conclusions: The data from the present experiment indicates that GN animals displayed increased motivation for sucrose reward as indicated by the PR schedule data. These results suggest that motivation for calorie rich foods and possibly drugs of abuse may be increased in those individuals gestationally exposed to tobacco smoke given that both reinforcers act on the mesocorticolimbic dopamine system.
Financial Support: NIDA Grant DA 021287

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NOVEL USE OF DOSE EQUIVALENCE THEORY TO EXAMINE COCAINE-INDUCED ENDOTHELIAL DYSFUNCTION.

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Aims: The aim of this project is to employ our novel methodology to produce quantitative descriptions of endothelium-dependent vasodilation (EDV) by agonists causing overt vasoconstriction, which will be used as a metric for examining the vascular consequences of chronic cocaine use. This methodology employs the theory of dose equivalence to derive the dose-effect relationship of the EDV induced concomitantly to vascular smooth muscle activation and vasoconstriction, which cannot be measured directly. This quantitative description of vasodilatory function is agonist-specific, and can be used to demonstrate endothelial dysfunction (ie, after chronic cocaine treatment). Clinical evidence suggests cocaine abusers are at increased risk of atherosclerosis and hypertension, which are both closely associated with endothelial dysfunction. To date, few studies have examined the vascular effects of cocaine abuse, or its influence on the effects of endogenous vasoactive mediators.
Methods: Aortae from adult male SD rats are excised for isometric tension measurments. Preparations include endothelium-denuded and –intact aortic rings, which allow for calculation of EDV components of angiotensin II (AngII) and endothelin-1 (ET-1). Chronic cocaine-treated rats (20 mg/kg i.p. daily for 14 days) are tested 24h following the final injection.
Results: In untreated rats, the dose-effect relationship for AngII in endothelium-denuded aortic strips is more efficacious compared to endothelium-intact strips (52.06 ± 3.07 vs 15.9 ± 2.52 % 120 mM KCl response) but equipotent (12.8 ± 4.21 vs 11.0 ± 5.31 nM EC50 values); while for ET-1, removal of the endothelium results in an increased potency (left-shift of EC50; 1.62 ± 0.31 vs 9.28 ± 4.3 nM) with no change in Emax (both approximately 100% 120 mM KCl response). Experiments with cocaine-treated rats are underway.
Conclusions: This functional measure of agonist-specific impairment of EDV is novel, and may provide a quantitative method of describing endothelial dysfunction.
Financial Support: This research was supported by NIDA grants T32-DA007237 and P30-DA013429.

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DISSOLVABLE TOBACCO: POISON CANDY OR METHADONE FOR SMOKERS?

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Aims: Reduced toxicity tobacco products may be useful in tobacco harm reduction. We examine two new dissolvable tobacco (DT) products for their toxic constituents and review poison control center data for cases of accidental pediatric poisoning with DT and other tobacco products.
Methods: DT products were analyzed for 40 harmful or potentially harmful (H/PH) constituents (FDA 2010), and compared to data for traditional smokeless tobacco (ST) products. Pediatric poisoning cases were identified from a review of the American Association of Poison Control Centers (AAPCC) annual reports from 1984-2008, and from an analysis of all "snuff" cases for all of 2009 and the first quarter of 2010.
Results: The majority of the FDA H/PH toxins were either non-quantifiable or below detectable limits in the new DT formulations. Carcinogens such as tobacco-specific nitrosamines and benzo[a]pyrene, and known toxins such as ammonia, lead, cadmium, and volatile nitrosamines, were either unmeasurable or substantially lower relative to traditional ST products. AAPCC data revealed that most ingestions of tobacco products were by toddlers, involved cigarettes, and were non life-threatening. Of 517 "snuff" cases in young children from Q1 2009 through Q2 2010, 3 (0.6%) were coded specifically as DT; each had either "no effect" or a "minor effect" and resolved with home care.
Conclusions: DT products contain very low levels of toxic constituents relative to cigarettes and conventional ST products, and are very rarely involved in pediatric poisonings. These products would reduce harm in habitual smokers unwilling or unable to quit, and for whom nicotine replacement therapy or prescription medication has not worked or is undesirable. Nonetheless, any smokeless tobacco product, however detoxified, would likely remain controversial in certain segments of the public health community, regardless of any significant reduction in toxin levels, given the experience over the years with other harm-reduction alternatives such as buprenorphine and methadone for the treatment of opioid dependence.
Financial Support: This work was funded by Rock Creek Pharmaceuticals, Inc., Gloucester, MA.

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EFFECTIVENESS OF OVERDOSE PREVENTION TRAINING: DIFFERENCES BETWEEN TRAINED AND UNTRAINED IDUS.

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Aims: Fatal opioid overdoses (OD) cause more than half of all deaths among injection drug users (IDUs), which far exceeds the proportion of deaths due to AIDS or other causes. Community-based programs have responded by developing OD prevention training, which include distributing naloxone to IDUs. Descriptive data are lacking on differences between IDUs who have received OD prevention training and IDUs who have not.
Methods: Study eligibility was based upon two primary criteria: current injection drug user; and witnessed a drug OD within the past 12 months. Sampling was stratified to enroll IDUs who had received OD prevention training from two community-based organizations in Los Angeles and IDUs who had not received training. Participants (n=99), 26 trained and 73 untrained, were recruited between March and October 2010. Interview questions focused on responses to witnessed OD, outcomes of witnessed OD, and patterns of substance use.
Results: Both trained and untrained IDUs were typically in their early 40s and largely white, African American, or Latino. Trained respondents were more likely to be female, to have recently experienced a drug overdose themselves, and to identify heroin as their drug of choice. In response to the most recently witnessed OD, trained IDUs were more likely to act as recommended by the training program, such as stimulating the victim with a sternum/nose rub, to perform rescue breathing, or to inject the victim with naloxone. Additionally, trained IDUs were less likely to perform behaviors that were not recommended, such as hit or slap the victim. None of the trained respondents reported that the OD victim died whereas 15% (n=11) of untrained respondents reported that the victim died.
Conclusions: IDUs who received OD prevention training were better prepared to effectively respond to a drug OD. Overdose prevention training programs should increase efforts to reach untrained IDUs.
Financial Support: This study is supported by NIDA (DA026789).

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HEPATITIS AND HIV KNOWLEDGE IN METHADONE PATIENTS.

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Aims: Drug users are at a high risk of acquiring HIV and viral hepatitis through drug and sexual behaviors. Knowledge surrounding prevention and treatment of these diseases is low in this population. Understanding predictors of Hepatitis and HIV knowledge in methadone maintained patients can help identify future targets of intervention.
Methods: Participants (N=488) were administered scales assessing knowledge of Hepatitis A, B, and C prevention and treatment as part of a multi-site randomized HIV-Hepatitis Care Coordination intervention. Other measures included a HIV knowledge questionnaire, the Addiction Severity Index, and the SF-36. Assessments occurred at baseline, 3, 9, and 12 months. Only baseline measurements are presented.
Results: Our sample was 31% Hispanic, 29% African American, and 36% Caucasian, 68% male and 91% heterosexual. Participants scored lowest on Hepatitis A (Mean=58.88% SD=18.12) and highest on the HIV knowledge tests (Mean=83.91 SD=11.05). Predictors of baseline knowledge scores were explored. Hispanics and African Americans had lower scores than Caucasian participants on Hepatitis C (Hispanics $t=-3.69$, $p<.001$; African Americans $t=-5.75$, $p<.001$) and HIV knowledge scales (Hispanics $t=-3.00$, $p<.05$; African Americans $t=-5.05$, $p<.001$). Other predictors of reduced HIV knowledge included marginal housing ($F\ 1,484=8.45$, $p<.05$) and self reported positive Hepatitis C status ($F\ 1,361=5.49$, $p<.05$). Individuals with marginal housing also had lower Hepatitis C scores ($F\ 1,484=4.47$, $p<.05$). Older individuals showed lower Hepatitis C ($r=-.11$, $p<.05$) and HIV ($r=-.22$, $p<.001$) knowledge scores than younger individuals. Gender, HIV status, and sexual orientation were not significant predictors.
Conclusions: Participants were knowledgeable about HIV transmission and treatment and less knowledgeable about Hepatitis A, B, C. Interventions should focus more on educating drug users on how these diseases are transmitted and target ethnic minority and homeless individuals.
Financial Support: NIDA Grants (R01DA20781, R01DA020841, P30 DA 011041, P50DA009253 & U10DA15815)

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CULTURAL CONSIDERATION IN TREATING ETHNIC MINORITY MSM.

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Aims: The CDC estimates that one in five MSM is HIV-positive, with nearly half (44%) unaware of their infection, and ethnic minorities disproportionately affected (CDC, 2010). The goal of this project was to gather formative data from service providers and clients to guide the development of an on-line training curriculum targeting providers working with ethnic minority men-who-have-sex-with-men (MSM) who have HIV/AIDS or are at risk for becoming infected. Data will advance cultural understanding of and preparation to effectively and sensitively provide services to African-American, Latino, Asian/Pacific Islander, and Native American substance-using MSM at risk.
Methods: Four research teams conducted 15+ focus groups (FG) in 6 states and the D.C.-metro area with more than 100 clients from the targeted ethnic groups and providers from agencies serving target group. The discussions were recorded and transcribed verbatim. Each research team analyzed the content of their transcripts and identified recurring themes.
Results: FG findings identified distinct substance use preferences/patterns and sexual behaviors/risk by ethnic group. Despite differences, common themes discussed among ethnic minority MSM and providers were issues of shame and stigma associated with sexual behavior, rooted in both religion and culture; ethnic identity as both a strength and a barrier to accessing services; acculturation and power issues in partner selection and perception of risk; on-going tension between ethnic and gay identities; feelings of social and sexual isolation; lack of minority role models; a sense of duty to family; and familial pressure to enter into heterosexual relationships, have children and continue the family name.
Conclusions: Cultural distinctions exist within the MSM community that should be considered as service providers deliver appropriate and sensitive services addressing the needs of substance-users who are HIV-infected or at risk.
Financial Support: Supported by SAMHSA #5UD1 TI13594-07S3

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PROSPECTIVE PATTERNS AND CORRELATES OF QUALITY OF LIFE AMONG WOMEN IN SUBSTANCE ABUSE TREATMENT.

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Aims: Quality of life (QOL) is a key dimension of addiction recovery. However, we know little about patterns or predictors of QOL. This study (1) Describes overall QOL and key components (physical, emotional, social and environment) at intake; and (2) Explores predictors of QOL changes over time.
Methods: Women (N = 206) in 3 treatment programs were assessed 1 week (T1), 1 and 6 months post-intake (T2 and T3). Standardized measures included the World Health Organization QOL BREF, Computerized Diagnostic Interview Schedule, Social Support for Recovery and Friends Support for Abstinence Scales. Abstract presents T2 data (89% retention); anticipated full T3 at CPDD conference N = 150. All findings significant at $p<.05$.
Results: Participants were 61% African American with a mean age of 37 years. Most (74%) were dually diagnosed (DD); 51% were dependent on alcohol, 62% on cocaine; 64% had >2 dependencies. At T1, physical, emotional and social QOL were significantly poorer among DD ($r = -.25$); older age and having a partner were significantly associated with better social QOL ($r = .144$ and $r = .271$, respectively). Only physical and emotional QOL improved at T2 ($t = -2.769$ and -4.364). Controlling for T1 QOL scores, outpatient (vs. residential) treatment ($\beta = -.126$) and DD status ($\beta = -.120$) predicted poorer physical QOL, while recovery support ($\beta = .191$) and friend support ($\beta = .124$) predicted better emotional QOL.
Conclusions: Understanding in-treatment QOL changes and their predictors can inform service delivery. Enhancing support networks may contribute to better emotional QOL. Results suggest interventions are also needed to enhance social and environment QOL for women in recovery as impairments persist.
Financial Support: Supported by: NIDA R01DA022994

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FINDINGS FROM A THREE-YEAR FOLLOW-UP STUDY OF THE FIRST SUBSTANCE ABUSE PREVENTION AND TREATMENT PROJECT AT AN INSTITUTE OF HIGHER EDUCATION IN ISRAEL.

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Aims: Epidemiological studies conducted by the Israeli Anti-drug Authority (IDA) indicate that 26% of the students in institutions of higher education in Israel reported illicit drug use (mainly Cannabis) at least once in the past year. These studies also revealed that 66% of Israeli students have very permissive views of illicit substance use, and 42% said that they would consider trying Cannabis. Research both on the international level and in Israel points to students as a population at risk for substance abuse. Many institutions of higher education around the world offer their student population prevention and treatment services. Such services were previously not offered in Israeli universities or colleges. This situation led us to offer a prevention and treatment project at the Tel-Hai Academic College in Northern Israel.The project began in the academic year 2007-2008. The project operates on three levels: broad base prevention activities, treatment for students with substance abuse problems and follow up research.
Methods: Standardized questionnaires developed by the Israeli Anti Drug Authority were used. The questionnaire is designed to follow students attitudes towards and use of psychoactive substances. The questionnaire was administered to most first and third year BA students of the College. Three points of time were used; at the imitation of the project, at the beginning of the second academic year and at the end of the third year.
Results: Baseline findings from the first two years (n=1400) indicate that views and use of illicit substances among students at Tel-Hai are slightly lower than the average Israeli student. The project and its study findings from the three-year follow-up will be presented and discussed in detail.
Conclusions: Implications for future research and policy will be discussed.
Financial Support: Support of the Rashi Foundation.

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EFFECTS OF VARENICLINE AND REINFORCING ABSTINENCE WITH AN ALTERNATIVE NONDRUG REINFORCER ALONE AND IN COMBINATION ON NICOTINE SELF-ADMINISTRATION IN RATS.

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Aims: Preclinical animal models for developing medications for drug abuse often fail to incorporate behavioral contingencies that are used to promote abstinence in clinical trials for medications, perhaps limiting the predictive validity of animal models. The objective of this experiment was to begin to address this issue by examining the effects of varenicline in an animal model of contingency management (CM) interventions, which employs a differential-reinforcement-of-alternative-behavior (DRA) schedule of alternative nondrug reinforcement.
Methods: Sprague-Dawley rats were trained to self-administer nicotine (0.03 mg/kg/inf) under a fixed-ratio (FR) 3 schedule of drug delivery. After stable nicotine self-administration (NSA) was obtained, rats were exposed to daily varenicline injections (1.0 mg/kg) or an interlocking DRA schedule of sucrose delivery + saline pretreatment for five consecutive sessions (tested in counterbalanced order across rats). Under the DRA schedule, nicotine continued to be available under the FR schedule while a sucrose pellet became available contingent upon every pause in NSA responding of 160 sec, at which point a pellet was delivered if the sucrose lever was pressed. Rats were then exposed to the DRA schedule + varenicline for five consecutive sessions, followed by a retest of varenicline and the DRA schedule alone (five sessions each).
Results: The DRA schedule and varenicline alone significantly, but only partially (34 an 30%, respectively, $p<0.01$), reduced NSA. Combination of varenicline and the DRA schedule produced a greater suppression of NSA (74%, $p<0.001$) compared to both the first and second test of each treatment alone.
Conclusions: These findings are consistent with clinical studies showing that combing CM with medication can be superior to either type of treatment alone for promoting abstinence. By motivating abstinence via behavioral treatment, the present CM model may provide a preclinical platform for medications development that is more analogous to clinical trials in humans.
Financial Support: NIDA grant DA020136

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PRIZE-BASED CONTINGENCY MANAGEMENT AND STANDARD TREATMENT FOR SMOKING CESSATION.

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Aims: This study had two primary aims: 1) Assess the efficacy of prize-based contingency management (CM) for smoking cessation compared with Standard treatment (ST); and 2) compare the differential efficacy of two reinforcement schedules (Traditional and Early Enhanced).
Methods: Smokers (N = 80 randomized to one of 3 conditions) participated in a one-week baseline and a four-week treatment. Participants in the CM conditions earned escalating chances to win prizes for negative carbon monoxide (CO; <6ppm) and cotinine (<100ng/ml) samples. Traditional CM participants had a 50% chance of winning a prize with each draw. Enhanced participants had a 100% chance of winning a prize with each draw during week 1 and 34% chance during weeks 2-4. ST participants received a small payment contingent on attendance.
Results: We compared CM participants (combining both CM conditions) to ST participants on CO levels using Generalized Estimating Equations (GEE). The baseline GEE model comparing CM (Mean (standard error) = 12.2(0.6)ppm) and ST (M(SE) = 12.1(1.8)ppm) CO levels was not significant ($p = .94$), but the GEE model comparing treatment phase CM conditions (M(SE) = 5.2(0.5)ppm) to ST (M(SE) = 9.7(1.8)ppm) CO levels was significant ($p < .02$) indicating that CM participants significantly decreased CO levels relative to ST participants. We then compared participants who received Traditional CM to those who received Enhanced CM. The GEE model comparing baseline CO for Traditional (M(SE) = 11.2(0.8)ppm) and Enhanced (M(SE) = 13.1(0.9) ppm) conditions was not significant ($p = .12$). Nor was the GEE comparing treatment phase CO levels for the Traditional (M(SE) = 4.6(0.8) ppm) and Enhanced (M(SE) = 5.6(0.7) ppm) conditions ($p = .39$), suggesting that, overall, the Early Enhanced condition did not have an advantage over the Traditional CM approach.
Conclusions: Our findings suggest prize CM is an efficacious smoking reduction treatment.
Financial Support: Supported by NIH grant DA021839 and Joe Young, Sr. Funds (State of Michigan).

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MARIJUANA SELF-ADMINISTRATION IN HIGH- AND LOW-IMPULSIVE SENSATION SEEKERS USING A MODIFIED PROGRESSIVE-RATIO PROCEDURE.

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Aims: Individual differences in sensitivity to drug reinforcement have been related to sensation- seeking status. High sensation seekers report using marijuana at an earlier age and in greater amounts, but individual differences in sensitivity to the behavioral effects of THC as a function of sensation-seeking status have not been examined. This ongoing study examines THC self-administration using a modified progressive-ratio procedure in low- and high- impulsive sensation seekers.
Methods: Twenty-three of forty young adult marijuana users scoring in the upper and lower median split of population norms on the impulsive-sensation seeking subscale of the Zuckerman-Kuhlman Personality Questionnaire have completed the 8-session 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: A preliminary analysis indicates that the number of earned puffs increases as a function of THC concentration (0%: 3.8 ± 2.8; 1.75%: 5.3 ± 2.7; 3.5%: 6.0 ± 1.8), demonstrating that THC functions as a reinforcer. At the 1.75% dose, significant group differences have emerged in the number of puffs earned (e.g., low SS: 4.1 ± 3.5; high SS: 5.9 ± 2.1), indicating that the reinforcing efficacy of THC is greater among high sensation seekers. In addition, high sensation-seekers report greater scores on several self-reports of the reinforcing effects of THC.
Conclusions: These preliminary results demonstrate that high sensation seekers are more sensitive to the reinforcing effects of THC.
Financial Support: Supported by DA-05312 and RR-15592.

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ARE ADOLESCENT ADDICTIVE BEHAVIORS ASSOCIATED WITH ADOLESCENT PREGNANCY?

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Aims: Adolescent fatherhood has been associated with increased delinquency and decreased life satisfaction. This study further explores adolescent fatherhood and its association with addictive behaviors, particularly adolescent gambling.
Methods: Data were from 294 males participating in a prospective cohort study that began when they entered 1st grade (86% African Americans, 81% of the original male cohort). Gambling behaviors between ages 16-20 were assessed via the South Oaks Gambling Screen-Revised for Adolescents and self-reports of impregnation assessed impregnation/fatherhood through age 20. Cumulative measures of early-onset conduct disorder, alcohol and illegal drug use (ages 13-16) were created. After time to event analysis, Cox regression models assessed the hazard of young impregnation by different gambling groups.
Results: By age 20, 34% of the adolescents had caused a pregnancy. Among fathers, 76% had gambled compared to 59% of never-fathered ($p<.05$). Twenty-nine percent of the ever-fathered were problem gamblers (PG) compared to 14% of the never-fathered ($p<.05$). Kaplan Meier curves showed that PG were more likely to have first impregnated at younger ages than nongamblers (NG) and social gamblers (SG; $p<.05$). By age 20, the cumulative hazard for impregnation was 20.8% (95% CI:13.9, 30.4%) for NG, 28.9% (95% CI=21.6%, 38.0%) for SG, and 54.3% (95% CI=41.2%, 68.5%) for PG. Subsidized lunches (proxy for socioeconomic status), conduct disorder, alcohol and drug use were also more prevalent among fathers. In Cox models gambling was associated with 70% increased hazard of fatherhood (95% CI=1.0, 2.9; $p<.05$) as were subsidized lunches (95% CI=1.1, 2.8; $p<.05$) and conduct disorder (95% CI=1.1,2.8; $p<.05$). PG had 2.5 times the hazard of impregnating as compared to NG (95% CI=1.2, 5.5; $p<.05$).
Conclusions: Our findings suggest that gambling, especially problem gambling, is related to adolescent pregnancy, adding to the existing evidence of the association between addictive behaviors and young fatherhood.
Financial Support: Study supported by RO1HD060072 (P.I.: Dr. Martins).

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A DISEASE RISK REDUCTION CURRICULUM FOR SUBSTANCE-ABUSING OFFENDERS.

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Aims: The purpose of the TCU Disease Risk Reduction (DRR) Project is to develop and test an intervention, *Waysafe*, designed to increase positive decision-making skills among offenders for healthy living, including skills for reducing disease risk behaviors. The project focuses on reducing risky sexual and drug use behaviors during re-entry by improving problem recognition, commitment to change, and strategies for avoiding behavioral risks of infections. *Waysafe* includes 6 one-hour motivational and planning sessions utilizing cognitive mapping strategies delivered near the end of CJ institution-based substance abuse treatment.
Methods: A total of over 500 incarcerated offenders receiving substance abuse treatment from eight different institutions in two states participated in the study. Pre- and post-test surveys included measures of knowledge, confidence, and motivation regarding general HIV information, risky sex and drug use, what to do if exposed, and general life skills. All participating offenders completed a pre-test survey and were then randomly assigned to the DRR *Waysafe* intervention or treatment as usual (TAU). At the completion of the six-week *Waysafe* curriculum, all participating offenders completed the post-test survey.
Results: Comparisons between the *Waysafe* and TAU groups at baseline showed only minor differences — the TAU group had a slightly higher score on General Knowledge and the *Waysafe* group had a slightly higher score on Desire for Change. The post-test survey showed significantly higher scores for the *Waysafe* group on all scales included in the survey.
Conclusions: Results supported hypotheses that offenders who completed the six *Waysafe* sessions, when compared to TAU, would have greater knowledge, confidence, and motivation about general HIV information, about risky sex and drug use activities, about what to do if exposed to HIV, general life skills, disease risk concerns, desire for change, and their perceptions about their HIV coursework.
Financial Support: Funding was provided by the National Institute on Drug Abuse, National Institutes of Health (NIDA/NIH) through a grant to Texas Christian University R01DA025885.

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ARE OREO COOKIES ADDICTIVE?

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Aims: We have been exploring the hypothesis that highly palatable foods can be as addictive as drugs of abuse by testing whether differences in sensitivity to the motivational properties of Oreo cookies assessed by conditioned place preference (CPP) are associated with differences in intravenous self-administration (SA) of cocaine.
Methods: For CPP, 80 non-food restricted, male Sprague-Dawley rats received 8 conditioning sessions with access to either a single Oreo in one compartment or no food. In Experiment I, eleven days following CPP, 48 rats were trained to self-administer cocaine (one 3h session/day x 8 days)followed by extinction (one 3h session/day for 11 days), and then by reinstatement precipitated by consumption of Oreos and by a cocaine prime (20 mg/kg IP). In Experiment II, 32 rats were trained to self-administer cocaine as above, and then break points (BPs) were assessed using a progressive ratio (PR) schedule. Experiment III (n=24) was identical to Experiment 1, but Oreos were replaced by a non-palatable food; plain rice cakes.
Results: In CPP, rats displayed either a preference, or no preference/avoidance for the Oreo-paired compartment, and this was not due to differences in the quantity of Oreos consumed during conditioning. During SA, "preference" rats displayed greater responding during extinction. At test, consumption of Oreos precipitated cocaine seeking in preference but not avoidance rats, and the cocaine prime was effective in both groups; however, the magnitude of reinstatement was greater in preference rats. In addition, preference rats displayed significantly higher BPs. Finally, rats also displayed a preference or no-preference/avoidance for a rice cake-paired compartment, however no group differences were observed during subsequent cocaine tests.
Conclusions: These findings indicate that greater sensitivity to the motivational properties of palatable foods may reflect individual differences in vulnerability to the reinforcing effects of drugs of abuse. Therefore, for some individuals, foods high in sugar and fat can be considered as "addictive" as cocaine.
Financial Support: New Emerging Team grant from Canadian Institutes of Health Research.

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AUTONOMY AND RELATEDNESS AMONG SUBSTANCE-USING MOTHERS AND THEIR CHILDREN.

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Aims: Children of substance using parents are at increased risk of experiencing negative outcomes both within and outside the family. A balance of self-reliance and familial togetherness, termed autonomous-relatedness, has been associated with positive outcomes in youth such as reduced substance use, depressive symptoms, and delinquency. Yet, research to date has primarily focused on autonomous-relatedness with youth who are substance users, or with non-using white, middle class families. The current study (n = 40 dyads) examined autonomous-relatedness in a sample of substance using mothers and their children. Autonomous-relatedness was expected to be negatively related to mother's substance use, and positively related to mother's romantic relationship quality and child's peer relationship quality.
Methods: Participants were recruited from a local outpatient treatment facility for substance users. Eligible participants were mothers with a child between the ages of 8-16 years, met DSM-IV criteria for substance abuse or dependence, and lived in the Columbus, Ohio, area. At baseline, mother and child completed self report questionnaires and participated in a brief observation task assessing autonomous-relatedness.
Results: Preliminary analyses using structural equation modeling techniques suggested that both mother and child's autonomous-relatedness was negatively related to mother's substance use (β = -.135, p = .031; β = -.388, p =.006, respectively). A statistical trend was found for the relationship between autonomous-relatedness and child's peer relationship quality.
Conclusions: This study supports previous research demonstrating a positive relationship between autonomous-relatedness in families and substance use. However, few studies have examined autonomous-relatedness in families with a substance using parent. Preliminary findings also provide evidence of inhibited social relationships outside the family system among children of substance users.
Financial Support: This work was supported by NIDA grant R01 DA023062.

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RURAL DRUG USERS' HIV RISK AND COMMUNITY CORRECTIONS INVOLVEMENT.

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Aims: U.S. studies consistently report that illicit drug users in the criminal justice system are more likely to be involved in HIV high risk behaviors and are HIV infected. However, little is known about HIV risk behaviors among active rural drug users in community corrections (CC) – drug users on probation, on parole, in pretrial release or diverted from prison. Consequently, the purpose of this study is to examine HIV risk behaviors among rural drug users by their CC involvement.
Methods: 400 rural drug users participating in a HIV risk study are examined. These current drug users are Appalachians age 18 or older who used one of the following drugs to get high in the past 30 days: prescription opioids, heroin, cocaine or methamphetamine. An interviewer-administered questionnaire was used to collect data including demographics, drug use, HIV risk behaviors and CC involvement.
Results: Participants are male (58.8%) and white (93.8%) with a mean age of 32.8. Risky behavior was high with 77% reporting injecting and 45.8% testing positive for HCV. Over one-fifth (22.9%) were CC involved. However, it was not expected that there would be only one significant difference for CC involved participants — CC involved participants were significantly more likely to have initiated someone into injection drug use (IDU) (p=0.003). There were no significant differences on other HIV risk behaviors including IDU, syringe sharing, number of sex partners, and unprotected sex with IDUs and/or while trading sex.
Conclusions: Among these very rural Appalachian active community drug users, the proportion of participants engaging in HIV risk behaviors is high, but similar regardless of CC involvement. Consequently, CC involved rural drug users do not differ from other rural drug users and should receive equity without stigma to participate in the limited rural community drug treatment as well as HIV services, which may not be a current reality.
Financial Support: Supported by 5RO1-DA24598.

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ASSOCIATION OF RISK PERCEPTION AND SUBJECTIVE NORM ON QUANTITY OF OPIOID PILLS MISUSED.

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Aims: We examined whether participants reporting a lower level of risk perception (RP) and a stronger subjective norm (SN) misused more prescription opioids (Rx-Opi) in the past year than those with a higher RP and a weaker SN.
Methods: Data were from 375 participants in St. Louis (STL) who reported misusing Rx opioids in the past year. RP and SN related to the Rx-Opi misuse were assessed by the Risk Behavior Assessment. For RP related to Rx-Opi use, participants indicated how dangerous they thought 'driving after taking a pain medicine' was, from not dangerous at all (1) to extremely dangerous (5). Additionally, participants indicated the most dangerous drug from a list of 13 drugs. For SN, participants estimated how many people, out of 100 in STL, misused Rx-Opi. A higher estimate indicated a stronger SN. Analyses: Negative binomial regressions were used to examine the associations between RP, SN, and the number of Rx-Opi pills misused in the past year.
Results: The sample was 57% male and 50% African American, with a mean age of 39 years. The median of past year Rx-Opi consumption was 123 pills. Participants perceived driving after pill use as dangerous (mean rating: 3.49). 57% of participants indicated that opioids were the most dangerous drug. Regression analyses showed that those who perceived lower risk associated with driving after pill use also reported a higher number of misusing opioid pills. However, those who ranked opioids as the most dangerous drug did not statistically differ from the others in terms of the quantity of opioid pills misused. Participants thought that nearly half (48%) of the people in STL are misusing Rx-Opi. Subjective norm was significantly associated with past year opioid pill misuse; the stronger the subjective norm, the more Rx-Opi pills misused.
Conclusions: Our hypothesis about the association between risk perception, subjective norm, and past year Rx-Opi misuse was generally supported. These findings provide important information to help future research on risk perception, subjective norm, and Rx opioid misuse.
Financial Support: NIDA

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PSYCHOMOTOR AGITATION IN SUBSTANCE DEPENDENCE.

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Aims: Depression with psychomotor agitation (PMA; "agitated depression") is a putative psychiatric phenotype that appears to associate with some forms of substance dependence. However, it is unclear whether such relationships extend across different substances and independent (I-MDE) versus substance-induced (SI-MDE) subtypes of major depressive episodes. We examined whether lifetime depression with (vs. without) PMA was associated with lifetime substance dependence across individuals with lifetime: (1) I-MDE only (n = 575); and (2) SI-MDE only (n = 1683).
Methods: Data were pooled from several family and genetic studies of substance dependence in which participants received identical structured interviews to diagnose DSM-IV mental disorders.
Results: In I-MDE, PMA was associated with alcohol, cocaine, opioid, other drug (hallucinogen, inhalant, speed-ball), and sedative dependence. After controlling for demographic and clinical co-factors, PMA's relationship to opioids, other drugs, and sedative (but not alcohol or cocaine) dependence remained significant. In SI-MDE, PMA was associated with alcohol, cocaine, opioid, and other drug dependence. After adjusting for co-factors, associations remained significant for cocaine and opioids, but not alcohol or other drugs. While PMA-opioid relations were stronger in I-MDE than SI-MDE, depression subtype did not moderate relations of PMA to non-opioid forms of substance dependence.
Conclusions: Agitated depression associates with certain forms of substance dependence and it is unlikely that this comorbidity is solely explained by a unidirectional mechanism whereby drug use induces agitated depression.
Financial Support: This work was supported by NIH grants R01DA12849, R01DA12690, R01DA018432, K08DA025041, R01AA11330, P60AA03510, K05AA017435, and K24 AA13736, and the U.S. Department of Veterans Affairs.

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ACCURACY OF A METHOD TO QUANTIFY ILLICIT INTAKE OF METHAMPHETAMINE FROM URINE.

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Aims: Qualitative urinalysis can verify abstinence of drug misuse but cannot detect changes in drug intake. Using non-pharmacologic doses of deuterium-labeled l-methamphetamine (l-MA-d3) we have developed a simple, robust method that accurately estimates changes in MA intake from spontaneously voided urine specimens.
Methods: Twelve subjects received 5 mg l-MA-d3 daily; after reaching plasma steady state they were challenged with 15, 30 and 45 mg of non-labeled d-MA. We used linear discriminant analysis to test if the urine concentration ratios of d-MA to l-MA-d3 differentiated between administered doses of d-MA. Classifier accuracy was evaluated by subject-based leave-one-out cross-validation and McNemar's test.
Results: 589 urine samples were collected; 331 between 0-24 hours and 238 between 24-48 hours post d-MA. For urine samples collected from the end of d-MA dosing through the next l-MA-d3 dose, the classification accuracy was 91% using the urine concentration ratio, which was a significant ($p<0.001$) improvement over the 54% accuracy using d-MA urine concentration alone. Classification based on both urine concentration ratios and time since dosing further improved accuracy to 96% ($p<0.001$). From 24-48 hours classifier accuracy using the urine concentration ratio falls to 60.0% for 15 mg dose differences but if the analysis is restricted to 30 mg dose increments accuracy remains robust at 84.6% and is a significant improvement over the 72.8% accuracy obtained using d-MA urine concentration alone ($p<0.01$). From 24-48 hours, including time as a predictor does not significantly improve classification accuracy (83.4%, $p=0.77$).
Conclusions: Using this method detection of as little as 15 mg changes in intake of MA is possible from random urine samples. The method can be used to quantify patterns of MA abuse and is amenable to deployment in clinical trials.
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GENOME-WIDE ASSOCIATION STUDY OF ADDICTION TO SMOKING AND OTHER SUBSTANCES OF ABUSE.

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Aims: Addiction to smoking and other abused substances is a common chronic disorder that is extremely costly to the individuals and society. Although genetics contributes significantly to vulnerability to these affective disorders, the susceptibility genes underlying them are largely unknown.
Methods: To identify susceptibility loci and genes for these addictive disorders, we conducted a case-control-based genome-wide association study for each target addiction on the GENEVA SAGE and NINDS datasets. The phenotypes of interest included addiction to smoking that was measured by Smoking Quantity (SQ), Smoking Urgency (SU), and Fagerström Test for Nicotine Dependence (FTND), and dependence on nicotine, alcohol, marijuana, cocaine, or opiates, which was measured by DSM-IV scales. A total of 3,015 subjects were considered; the number of cases affected by the various addictions differed. We also studied 1,465 controls, who showed no addiction to any licit or illicit drug.
Results: At the individual SNP level, 523, 528, 513,520, 559, 473, 515, and 457 SNPs showed association with SQ, SU, FTND, and dependence on nicotine, alcohol, marijuana, cocaine, or opiates, respectively, at a P value of $\leq 5\times10\text{-}4$. On the basis of the location of each SNP, 179, 178, 153, 167, 168, 167, 166, and 148 genes for these measures were identified. Among them, genes in chromosome 1 open reading frame 107, contactin 1, GDP-mannose 4,6-dehydratase, and Sp2 transcription factor were shared by all addictive measures. For smoking addiction, we identified 70 genes shared by all measures of ND. Further, 13 genes were common to the illicit drug addiction measures marijuana, cocaine, and opiates.
Conclusions: Although identification of SNPs and genes associated with specific drug addictions is still in an early stage, the utilization of GWAS approach for multiple addictions has provided an opportunity for understanding genetic mechanisms underlying each of these addictive disorders.
Financial Support: This study was supported by NIH grants DA-12844 and DA-13783.

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PRIMING EFFECTS OF DOPAMINE D1 RECEPTOR AGONIST ON THE REINSTATEMENT OF AMPHETAMINE-INDUCED CONDITIONED PLACE PREFERENCE.

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Aims: Relapse to drug use after a period of abstinence is a major feature of drug addiction and remains as a core issue in clinical treatment. A growing body of research using animal models has devoted to elaborating the neural mechanisms of drug reinstatement behavior. Previous studies revealing this drug seeking behavior mostly relied on using the self-administration, while less was conducted in using the conditioned place preference (CPP) model. The present study, thus using the amphetamine induced CPP, investigated the dose effects of amphetamine on the reinstatement. We further examined whether the dopamine D1 receptor agonist, SKF38393, would be able to prime the reinstatement of amphetamine CPP.
Methods: Following our previous work (e.g. Liao, 2008), CPP was formed by amphetamine with dosing given at 1 mg/kg (IP). The rats were then subjected to the extinction phase, which was consisted of 8-day exposure to the CPP test apparatus and following by a 3-day of staying in the home cage as the withdrawal. No injection was conducted in the extinction phase. The drug reinstatement tests were conducted 24 hr after the end of extinction phase.
Results: Amphetamine CPP was significantly demonstrated in all groups. The data, as measured over the 2nd, 4th, 6th, and 8th day of extinction, show that the amphetamine CPP was significantly extinguished after the present regimen of extinction. The doses of amphetamine (0, 0.5, and 0.75 mg/kg) were then evaluated in the drug-induced reinstatement test. A dose-related fashion was confirmed for amphetamine reactivating the extinguished CPP. In a separate experiment, SKF38393 (0, 0.1, 0.5 mg/kg) was tested for its priming effect on the reinstatement of amphetamine CPP. Only the high dose of SKF38393 could reinstate the amphetamine CPP.
Conclusions: These results, together, suggest that the reinstatement of amphetamine CPP is depended in dopamine D1 receptors.
Financial Support: National Science Council, Taiwan

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GABA MODULATION OF THE DISCRIMINATIVE-STIMULUS EFFECTS OF THC IN HUMANS.

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Aims: Cannabis remains the most commonly used illicit drug, and regular use can lead to dependence. Medications development efforts for cannabis-use disorders are ongoing, but no effective compounds have been identified. Neuroanatomical, neurochemical and behavioral pharmacology studies indicate a functional link between GABA and cannabinoid systems. The present studies test the hypothesis that administration of GABA drugs that vary in their mechanism of action will modify the effects of THC in humans, in an effort to screen potential medications using rational procedures based on the neuropharmacology of cannabis. The primary outcome is the interoceptive cue produced by THC as determined using a drug-discrimination procedure, which is a sensitive means to detect neuropharmacological interactions.
Methods: Subjects who report regular cannabis use are enrolled as outpatients and learn to discriminate oral THC. During a sampling phase, subjects receive 30 mg THC, identified by letter code (e.g., Drug X). During a control phase, subjects are required to correctly identify when they receive placebo (i.e., Not Drug X) or 30 mg THC. Finally, a test phase is conducted in which THC (0, 5, 15 and 30 mg) is administered alone and in combination with the GABA-A positive modulator diazepam (5 and 10 mg), the GABA-B agonist baclofen (25 and 50 mg) or the GABA transport inhibitor tiagabine (6 and 12 mg). Each drug is tested in a separate study, and between 6-8 subjects completed each study. Supplemental measures include self-report questionnaires, cognitive/psychomotor performance tasks and physiological indices. Data are analyzed using repeated-measures ANOVA.
Results: The discriminative-stimulus and other behavioral effects of THC are significantly enhanced by baclofen and tiagabine, but unaffected by diazepam.
Conclusions: These results indicate that GABA-B agonism and elevation of synaptic GABA modulate the clinical effects of THC, and provide targets for subsequent medications development research.
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INVESTIGATING CHANGES IN FRACTIONAL ANISOTROPY IN WHITE MATTER OF METHAMPHETAMINE USERS USING DIFFUSION TENSOR IMAGING.

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Aims: Methamphetamine addiction is an epidemic of global proportion and its consequences have become a major international health problem. Diffusion tensor imaging (DTI) studies in methamphetamine users have found reductions in fractional anisotropy (FA) in frontal and parietal white matter, suggesting axonal injury or altered myelination due to methamphetamine use. This study aimed to determine the effect of current methamphetamine use on FA in white matter using DTI.
Methods: Imaging was undertaken on a 1.5T Siemens Magnetom Avanto System using a diffusion-weighted echo-planar imaging sequence with b=0, 1000s/mm2 and 30 directions. Data were acquired from 17 methamphetamine-dependent participants aged 22-46, and compared with 20 healthy controls using the FDT, TBSS and Randomise toolboxes within FSL 4.1. Two-tailed unpaired t-tests – co-varied for age and gender, and corrected for multiple comparisons – were used to determine differences between methamphetamine-dependent participants and controls ($p<0.05$).
Results: Statistical analysis found no significant differences in FA of white matter between methamphetamine-dependent participants and controls.
Conclusions: Previous DTI studies in methamphetamine-dependent participants reported reductions in FA in some frontal white matter regions. However, no significant differences in FA between methamphetamine-dependent participants and controls were found in this trial. The lack of diffusion abnormalities may be due to different white matter changes resulting in opposing effects on FA – for example, increased water volume associated with neuroinflammation may lead to decreased diffusion while axonal damage or myelin degradation may lead to increased diffusion, leading to minimal or no significant net differences.
Financial Support: School of Pharmacy, University of Auckland

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COMPULSIVE DRUG-TAKING BEHAVIOR: INTERACTION OF SPECIFIC GENETIC VARIANTS WITH RESPONSE TO COCAINE VACCINE ON TREATMENT EFFECTIVENESS IN COCAINE DEPENDENCE.

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Aims: To explore potential genetic predictors of compulsive drug seeking behavior. Subjects treated with the cocaine vaccine but continue to self-administer cocaine may provide a 'real-world' model of the progression to compulsive drug taking. The cocaine vaccine is a promising biological intervention that alters the pharmacokinetic and pharmacodynamic properties of cocaine in a manner that reduces its reinforcing effects.
Methods: This 24 week double-blind placebo-controlled trial randomized 115 methadone maintained subjects to vaccine or placebo. Of the 55 subject in the cocaine vaccine condition, 34 also consented to genetic testing and were included in the current analysis. Genetic variants shown to be involved in drug addiction, specifically the dopamine and serotonin receptors involved in compulsive behaviors, were genotyped and evaluated.
Results: Treatment responders (n=16) were defined as those subjects randomized to the vaccine condition, who submitted more than 15% cocaine-free urines during the active treatment phase ('non-responders'; n=18). Significant interactions of specific variants and treatment effectiveness were found. The most significant findings were with variants in DRD2 ($p<0.05$), DBH ($p<0.01$), and OPRK1 ($p<0.05$).
Conclusions: Addiction to cocaine is a chronic, relapsing brain disease with severe medical, social, and economic consequences. The risks involved in becoming cocaine dependent are complex and include a substantial genetic influence. Identifying individuals with increased vulnerability to develop compulsive, drug taking behavior may improve treatment outcome by identifying mechanisms of actions in behavioral and pharmacological interventions that contribute to treatment effects.
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IMMEDIATE REWARDS IMPROVE OUTCOMES FOR METHAMPHETAMINE ADDICTION: A BEHAVIORAL ECONOMIC ANALYSIS OF A CONTINGENCY MANAGEMENT TREATMENT PROGRAM.

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Aims: Contingency management is an effective methamphetamine substance abuse treatment. This study applies behavioral economic principles to examine features of purchases made with these payments to elucidate the ability of contingency management payments to yield positive outcomes in treatment for methamphetamine dependence. We contrast the use of contingency management payments as a hedonic substitute for drugs with the use of payments as a positive reinforcement/reward.
Methods: In a randomized, controlled trial of methamphetamine-dependent gay men, 78 participants were randomly assigned to receive contingency management payments as part of a larger trial of behavioral treatments. The frequency, magnitude, and type of purchases (e.g. hedonic or utilitarian) made with the contingency management payments were assessed. Regression of purchase features on treatment outcomes assessed preferences for redemption as reflecting an economic hedonic substitute.
Results: Controlling for the number of days where money was available to be redeemed, participants who redeemed their payments for purchases more often were more likely to provide negative urine samples than those who redeemed purchases rarely ($b=0.479$, $p<0.001$). Further, participants who spent more of their money during the study rather than saving until the end of the study were more likely to have negative urine samples ($b=0.330$, $p<0.003$).
Conclusions: The frequency of redemption of payments for goods signaled positive treatment outcomes in this voucher-based CM program. Moreover, redemption of payments for certain goods may act as a hedonic substitute for substance use. Economic purchasing behaviors adopted in voucher-based CM treatments may support recovery during, and perhaps after treatment.
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HOMELESSNESS AND INJECTION DRUG USE AMONG A COMMUNITY-BASED COHORT OF INJECTION DRUG USERS IN BALTIMORE, MD, 2005-2009.

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Aims: Housing instability has been associated with HIV seroconversion and adverse HIV treatment outcomes. We assessed the temporal association between homelessness and ongoing injection drug use in a cohort of injection drug users (IDUs).
Methods: Participants included 1268 current and former IDUs recruited into the AIDS Linked to the Intravenous Experience (ALIVE, Baltimore, MD) and in follow-up in 2005-09. Information on demographics and risk behaviors was obtained using structured questionnaires. The association between reported homelessness (lagged one visit to ensure temporality) and injection drug use (heroin, cocaine, and/or speedball) was assessed using a random effects model. Stratified analysis was performed to assess the difference in association for those who were and were not injecting at the lagged visit.
Results: 66% were male, 87% African American, 77% were 35-54 years of age, and 54% reported injecting within the prior 6 months. After adjustment for demographics, risk behaviors, and health conditions, injection drug use was more common among participants who reported prior homelessness compared to those who did not [AOR=1.44, 95% CI (1.04,1.98)]. This association differed by whether participants reported injecting at the prior visit. Among participants who were not injecting at the prior visit, injection drug use was more common among participants reporting prior homelessness, though this association was not statistically significant [AOR=1.59, 95% CI (.96, 2.66)]. Among participants injecting at the previous visit, injection drug use was not associated with prior report of homelessness [AOR=.88, 95% CI (.63, 1.22)].
Conclusions: Homelessness appears to be a determinant for relapse into injection among those who have stopped injecting, a mechanism which may partially explain the link between homelessness and adverse outcomes related to HIV. Drug treatment programs should refer or directly provide housing assistance to improve client outcomes.
Financial Support: NIDA DA12568, DA04334

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THE GEOGRAPHY OF DRUG ARRESTS, VIOLENCE AND ALCOHOL IN BOSTON.

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Aims: We examine the relationship between drug markets and violence in the city of Boston in 2008 and determine what geographic/environmental and individual factors are related to the production of violence.
Methods: Data from the Boston Police Department, the census, survey data on neighborhood collective efficacy and Massachusetts state data on alcohol outlet type and location are used. Spatial modeling is employed and maps of hot spots for violence and drug markets are produced. Target and adjacent areas are also analyzed
Results: Areas with high rates of violence were associated with high levels of drug trafficking arrests, high densities of liquor stores (b=.624, p=.04) and bars (b=.742, p=.03) and were related to increased percentage of single mothers (b=0.453, p=.03), as well as neighborhood disadvantage (b= .63, p=.05) and collective efficacy (b=-1.43, p=.042). Model based hot spots for higher than expected levels of violence were also identified. These hot spots were found to have higher levels of drug arrests, proximity to liquor stores and lower collective efficacy. We also found that target area violence was related to adjacent area drug arrests.
Conclusions: areas with high rates of violence are also places where there is increased drug market activity controlling for alcohol outlet (type and density), collective efficacy and neighborhood disorganization.
Financial Support: This research is supported by a grant from NIAAA R21 AA018204-01

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MEASURING THE MEASURE: DOES THE VA SUD COC PERFORMANCE MEASURE ACTUALLY MEASURE CONTINUITY OF CARE?

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Aims: To assess the Veterans Administration substance use disorder (SUD) continuity of care (CoC) performance measure (PM), which scores retention during a three month observation period for patients qualifying for a treatment episode, for the Philadelphia VAMC Addiction Recovery Unit's (ARU) standard 6 month Intensive Outpatient Program (IOP).
Methods: The VISN Support Services Center (VSSC) tabulated 479 patients entering the Philadelphia VAMC SUD CoC PM for one year. Over 10,000 progress notes for these patients were reviewed by an automated text analysis, implemented in Microsoft Access using COM interface to DHCP (Vista) as previously reported to this meeting. Included were over 250 Brief Addiction Monitor (BAM) ratings.
Results: Of the 273 patients who failed the measure, 17% (47 patients) were registered by ARU staff as actively enrolled in the ARU IOP after the measure's observation period had closed – averaging 8.3 visits in the three months after the CoC measure was closed, and 15.0 visits after that. Only 5 of these patients qualified as "re-enrolled" by the CoC measure itself.
Conversely, of the 206 patients passing the measure, 35% dropped out of the IOP (2.4% for documented relapse), as indicated an absence for over 90 days or by formal discharge (Reason of Discharge: e.g., "rejected care", or "dropped out"). Only 28.2% were rated as "Treatment Complete" by staff; the bulk of the remainder continue in the IOP program as of this writing.
Conclusions: Harris (J. Sub. Abuse Treatment 2009; 36: 294) has reported that the VA SUD CoC may not accurately reflect treatment outcome. Here, we suggest that the current SUD CoC may have limitations in measuring the continuity of care itself, incorrectly classifying patients as "failed" who successfully engaged, and as "passed" who were judged by clinical staff to have disengaged from treatment. Time and space permitting, we will comment on potential improvements to the CoC, as for example, on the potential of the BAM ratings to clarifying patients' trajectories through the IOP treatment process.
Financial Support: CESATE - 2010-2011

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RELATIONSHIP BETWEEN EXTINCTION OF ATTENTIONAL BIAS TO COCAINE-RELATED STIMULI AND THE SEVERITY OF COCAINE DEPENDENCE.

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Aims: In recent studies, cocaine-dependent subjects showed attentional bias to cocaine-related stimuli. Preclinical studies demonstrated that response to cocaine-related stimuli was extinguished over repeated exposures. The aims of the present laboratory-based study were (1) to investigate changes in attentional bias to cocaine-related words over repeated exposure and (2) assess whether the extinction of attentional bias is related to the severity of cocaine dependence.
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 41 cocaine-dependent subjects. Attentional bias was defined as the difference between the reaction time to indicate color of cocaine-related words vs. that of neutral words (cocaine words – neutral words). The severity of cocaine dependence was measured by the number of positive diagnostic criteria for cocaine dependence on the Structured Clinical Interview for DSM-IV (SCID).
Results: We found that cocaine-dependent subjects showed significant attentional bias to cocaine-related words for the first block ($p < 0.05$) but that the attentional bias was not significant in 2nd-4th blocks. The mean attentional bias in the blocks 2-4 (but not block 1) was significantly correlated with the number of positive diagnostic criteria for cocaine dependence on the SCID (rho = 0.3151, p = 0.048, Spearman's rank correlation).
Conclusions: The results confirm our previous findings that that attentional bias is reduced as a consequence of repeated exposure to cocaine-related words. Additionally, the present data suggest that the smaller attentional bias over repeated exposures the less reported severity in cocaine dependence. Conversely, individuals who showed greater attentional bias to cocaine stimuli over repeated exposures were more likely to endorse greater dependence severity.
Financial Support: NIDA Grants P20 DA024157(Cunningham) P50 DA009262(Moeller)

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CAFFEINE AND ITS INTERACTION WITH NICOTINE-ASSOCIATED CUES IN THE PERSISTENCE AND REINSTATEMENT OF NICOTINE-SEEKING BEHAVIOR IN RATS.

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Aims: Caffeine and nicotine are the most commonly co-used psychostimulants. Clinical human studies and preclinical animal experiments to examine the direct effects of caffeine on nicotine intake have yielded equivocal results. Although there is a close temporal relationship of tobacco smoking (nicotine intake) with caffeine consumption, it is not known, however, whether caffeine invigorates nicotine-seeking behavior in an associative manner. This study examined the effects of caffeine on the extinction and reinstatement of nicotine-seeking responding in rats after nicotine self-administration training with caffeine exposure.
Methods: Male Sprague-Dawley rats were trained in 20 daily 1-h sessions to intravenously self-administer nicotine (0.03 mg/kg/infusion, free base) on an FR5 schedule and associate an auditory/visual cue with each nicotine delivery. Five min before these training sessions, rats received an intraperitoneal administration of 5 mg/kg caffeine. For the extinction tests, rats were tested under 4 conditions: pre-session caffeine, nicotine cue, caffeine+cue, or none. For the reinstatement tests conducted after extinction, rats were tested under 3 conditions: pre-session caffeine, nicotine cue, or both.
Results: Results showed that pre-session caffeine delayed extinction of and reinstated nicotine-seeking responding and that caffeine interacted with the nicotine cue to produce a stronger effect. Besides, in the rats trained without caffeine exposure, pre-session caffeine alone or combined with the nicotine cue also reinstated nicotine-seeking responding.
Conclusions: The results indicate a significant contribution of caffeine exposure to the persistence and reinstatement of nicotine-seeking behavior in both an associative and a non-associative manners as well as an interaction of caffeine exposure with nicotine cues that leads to heightened nicotine-seeking behavior. These findings suggest that abstinent smokers may benefit from stopping caffeine use.
Financial Support: Supported by NIH grant R01 DA17288 and startup fund from the University of Mississippi Medical Center.

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EFFECT OF ENVIRONMENTAL ENRICHMENT ON BEHAVIORAL PHENOTYPES AND METHAMPHETAMINE SELF-ADMINISTRATION IN RATS.

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Aims: Environmental enrichment (EE) during adolescence has been shown to produce protective effects against drugs of abuse, but it remains undermined whether EE during adolescence can alter the motivational effect of methamphetamine (METH) in adult rats. The recent study was designed to study the effects of EE on performance in the Morris Water Maze, locomotor activity, Vogel conflict drinking, conditioned freezing, and METH self-administration in rats.
Methods: Male Sprague-Dawley (SD) rats were raised in either EE or isolated environment (IE) from postnatal day 21 to 60. The influences of environmental modulation on various behavioral phenotypes were assessed. Another two groups of rats (EE or IE) were trained and maintained to daily self-administrate METH under a FR and FR schedule. D2 expression was detected in all the animals.
Results: IE induced a significant increase in body weight, the latent period and the unpunished clicks, compared with EE. The percentage of freezing was significantly lower in IE group than the one in EE group. In addition, environmental manipulation during adolescence also induced significant differences in the acquisition rate, drug consumption and break points. Finally, regional differences of dopamine D2 receptor expression were also evident between IE and EE group.
Conclusions: The present studies first demonstrated that EE can reduce the vulnerability to develop drug taking behavior and blunt the motivational effect of METH which might be mediated via dopamine D2 receptors.
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ORAL COCAINE REDUCE "CRAVING" IN COCAINE-DEPENDENT PATIENTS.

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Aims: There is no consensus on the term craving among specialists, but we can study if we consider it as a combination of intensity, frequency, duration and change in the desire for cocaine in cocaine dependent-patients. There are reports that oral cocaine use reduces the number of relapses in cocaine dependent-patients
Methods: Open trial with 10 volunteers, out-patient-dependents to inhaled cocaine/cocaine hydrochloride (IC) according to DSM-IV-R criteria, with average of 1.5 relapse per week in the last three months, range 1-2, avg 1 g per binge, all with positive benzoylecgonine (BE) in urine at entry were analyzed with the Cocaine Craving Scale/CCS/Halikas/1989 (questions 1 to 5). Five subjects ingested 50 mg of oral cocaine contained in coca tea three times a day during two weeks started one day after the last relapse. Five did not ingest cocaine or any oral medication, except advice.
Results: All 10 subjects attended 2 times a week to control and CCS test was applied. In oral cocaine group CCS levels decreased at first and second week. Levels in non-oral cocaine group remained unchanged. CCS indicate that oral cocaine group had significantly ($p < 0.05$) lower levels in the 5 points of CCS compared to those who did not ingest oral cocaine ($p \geq 0.05$). Subjects of the first group no relapse during study. Those who did not ingested oral cocaine relapse in the first and second week. All Subjects showed positive urine test at first and second week (there is evidence that subjects that ingesting oral cocaine always indicate a positive result in urine BE).
Conclusions: In conclusion, oral cocaine use reduces the levels of craving in cocaine dependent-patients, although remain positive BE urinalysis. These results suggest that oral cocaine can be used to reduce cocaine craving when starting treatment in cocaine dependent-patients.
Financial Support: Private financial support (Coca Medica Organization). No conflict of interest

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ARIPIPRAZOLE EFFECTS ON COCAINE PHARMACODYNAMICS AND COCAINE SELF-ADMINISTRATION IN HUMANS.

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Aims: Aripiprazole (AZ) is a unique atypical antipsychotic with partial D2 agonist activity. Human laboratory studies have shown that it attenuates the discriminative stimulus and subjective effects of d-amphetamine but results have been less promising with cocaine. The purpose was to evaluate the effects of AZ on subjective and physiological responses to cocaine and cocaine self-administration.
Methods: This 5-week inpatient, parallel-group study randomly assigned healthy, nontreatment-seeking adults who used cocaine regularly (≥ 2-3 times weekly) to oral AZ (0, 2 or 10 mg daily). For all groups, intravenous (IV) cocaine dose response and sample/choice self-administration sessions were conducted once each in the placebo lead-in, the acute and the chronic AZ dosing phases (12 sessions total). Cocaine (0, 20 & 40 mg/70 kg; IV, 1 hr apart) was given in dose response sessions; subjective, objective and physiologic measures were collected repeatedly after each dose. During self-administration sessions, subjects chose between the dose sampled earlier that day (0, 20 or 40 mg/70 kg; IV) or decreasing amounts of money for 7 trials (declining from $19 to $1 in $3 decrements).
Results: During the placebo-lead in, all subjects chose active cocaine doses more often than placebo cocaine. From placebo lead-in to chronic dosing, there was a statistical trend for the AZ 10 mg group to choose all drug conditions (including placebo) more often than money compared to the placebo-treated group. Over this time period, there were no significant effects of AZ dose on cocaine street value, desire, or bad effects; however, there was a significant effect of AZ dose on reducing reports of cocaine rush ($p<0.05$).
Conclusions: Despite all cocaine and AZ doses being safely tolerated, these data suggest AZ does not reduce the effects of cocaine and do not support AZ as a treatment for cocaine dependence.
Financial Support: NIDA R01 DA019433 (SLW) and UK Clinical Research Development and Operations Center

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ACCUMBENS DOPAMINE BI-DIRECTIONALLY REGULATES METHAMPHETAMINE-SEEKING IN MICE.

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Aims: Previous studies into the neurochemical effects of repeated exposure to low doses of methamphetamine have revealed that it sensitizes both glutamate and dopamine in the nucleus accumbens (NAC). Moreover, extended withdrawal from repeated methamphetamine treatment reduces accumbens basal dopamine but augments basal glutamate. The present study aims to examine the hypothesis that the changes in NAC dopamine might contribute to addiction-related phenomenon such as drug-seeking behavior.
Methods: Male C57BL/6J (N=20) mice were implanted with bilateral cannula (10mm, 20ga) directed towards the NAC (AP: +1.3, ML: ±1.0, DV: -2.3). The animals were then tested for methamphetamine-conditioned place preference (CPP) using an un-biased design in which 8 alternating pairings of saline and 2 mg/kg intra-peritoneal methamphetamine with two distinct environments. Animals were then assigned to treatment groups receiving intra-NAC vehicle (aCSF), the dopamine D2 receptor agonist quinpirole (12.9 ng/side) or the dopamine reuptake inhibitor GBR-12909 (26.2 ng/side) and received bi-lateral infusions immediately prior to a test for CPP.
Results: Vehicle-treated mice exhibited a significant methamphetamine-induced CPP, whereas the intra-NAC infusion of GBR-12909 doubled the magnitude of the CPP. In contrast, the intra-NAC infusion of quinpirole elicited a marked aversion to the methamphetamine-paired side.
Conclusions: These data indicate that NAC dopamine levels bi-directionally influences the expression of a methamphetamine-induced CPP. Pharmacological agents that elevate and reduce, respectively, extracellular dopamine levels potentiate and prevent methamphetamine-seeking behavior in this paradigm. These data point to the capacity of repeated methamphetamine to sensitize NAC dopamine as an important substrate in the manifestation of methamphetamine addiction-related behavior.
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IMPACT OF FIRST-WEEK MONETARY INCENTIVES IN A COMMUNITY SUBSTANCE ABUSE TREATMENT PROGRAM.

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Aims: AIMS: Despite the efficacy of Contingency Management (CM) the use of this evidence-based intervention is not widespread in community programs. The current study examined whether the administration of CM would improve two important outcomes for individuals with substance use disorders: 1) treatment utilization, and 2) drug abstinence from alcohol, marijuana, cocaine and opiates.
Methods: METHODS: A CM intervention was implemented as an adjunctive element of standard intensive outpatient treatment. Individuals who received the new CM protocol (n = 20; CM) were matched on demographic characteristics and compared to those admitted prior to protocol implementation (n = 20, control). Clients received a $10 gift card on day 2 of treatment (with intake as day 1), and a $15 gift card on day 5 of treatment. Baseline information was collected through a computer administered Addiction Severity Index. Treatment utilization and drug abstinence during the first 30 days of treatment were used to evaluate early treatment response. Treatment utilization (group or individual) was measured as a percentage (days attended divided by days available). Abstinence was measured as percentage of negative urinalysis screens during the initial 30 days of treatment.
Results: RESULTS: There were no significant differences between the CM and control groups on demographic or pre-treatment drug use characteristics. However, the CM group utilized significantly more treatment than the control group (p =.025; 70% versus 33%, respectively), and were more likely to test drug negative during the initial 30 days of treatment (p=.048; 71% versus 45%, respectively).
Conclusions: CONCLUSION: The CM protocol underscores the relevance and efficacy of CM for use in community practice. The intervention addresses a clear clinical need through a low cost intervention. A total sample of N = 120 from this ongoing protocol will be presented at the June meeting.
Financial Support: SUPPORT: No funding was received for this research.

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DOES DEPRESSION INTERFERE WITH CONTINGENCY-MANAGEMENT TREATMENT FOR PREGNANT CIGARETTE SMOKERS?

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Aims: Contingency management (CM) is efficacious in promoting smoking cessation in general populations (Volpp et al., 2009) and in special populations, including adolescents (Krishnan-Sarin et al., 2006) and pregnant women (Heil et al., 2008). Our group is researching the use of CM with pregnant smokers. One variable that predicts smoking cessation among treated pregnant smokers is depression (Ludman et al., 2000). The purpose of the present study was to examine whether baseline depression level (i.e., BDI scores) predicts treatment response among women receiving CM.
Methods: A sample of 157 pregnant women in controlled clinical trials examining the efficacy of CM was assigned to a contingent-incentive treatment condition (n = 80) or to a non-contingent control condition (n = 77). Baseline BDI scores did not differ between contingent and non-contingent women (10.29 ± 6.92 vs. 10.48 ± 6.61, p = .86). Associations between baseline BDI scores and smoking status were examined separately in each treatment condition at assessments conducted early and late in pregnancy using univariate and multivariate analyses.
Results: Baseline BDI failed to predict smoking status at either assessment in the contingent condition (early assessment: p = .34; late assessment: p = .44). Among those in the non-contingent control condition, baseline BDI was a significant predictor of smoking status at the early pregnancy assessment (smokers BDI 10.84 ± 6.60 vs. abstainers BDI 4.00 ± 1.83, p = .04), although not at the late pregnancy assessment (smokers BDI 10.72 ± 6.69 vs. 7.67 ± 5.28, p = .28).
Conclusions: In conclusion, we see no evidence that depressive symptoms interfere with a positive treatment response among those treated with CM even at an early-pregnancy assessment where elevated depressive symptoms predicted continued smoking in a comparable group of women who received a control treatment. Indeed, CM may help women surmount the adverse influence of depressive symptoms on smoking cessation.
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DRUG USE RESILIENCE AND ITS DETERMINANTS AMONG SCHOOL ADOLESCENTS IN BOGOTA, COLOMBIA.

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Aims: The growth of drug use among youth in developing countries is outpacing that in developed countries. Identifying factors associated with drug-use resilience (declining an opportunity to use drugs) is essential for developing effective prevention strategies, particularly in the Colombian context of high drug availability and scarce resources.
Methods: Data was collected from a cluster sample of 2,279 students from 23 schools in Bogota. Multilevel logistic regression models were implemented to estimate the effects of individual, familial and school level factors on drug-use resilience. Analyses were conducted among a subsample of 728 students who reported an opportunity to use drugs.
Results: Overall, 42.4% of students declined to use drugs when a first drug-use opportunity presented itself. Resilience rates varied by drug, being highest for cocapaste (69.3%) and ecstasy (55.7%) and lowest for marijuana (49.3%) cocaine (42.8%) and inhalants (41.1%). A sex difference in resilience was noted for marijuana only – 56.5% of girls vs. 44.5% of boys (p=0.011). Resilience rates were highest among students who reported a passive drug-use opportunity (46.3%) and lowest among those who reported an active drug-use opportunity (23.6%). The strongest predictors of drug-use resilience were not having drug-using first-degree relatives (Adjusted OR=4.01, 95%CI=2.0,8.1) and a high degree of parental supervision (AOR=2.38, 95%CI=1.4,4.3). Other predictors of resilience included a high perceived risk of regular drug use, not engaging in problematic behaviors, being a non-smoker, and studying in a school where drug use preventive education is common.
Conclusions: Familial, more than individual and school-contextual factors, are important in promoting drug-use resilience. Prevention strategies focusing on developing supportive parental relationships could be effective in slowing the growth of drug use among youth in Bogota and elsewhere.
Financial Support: C. Lopez-Quintero was funded by a Milstein Doctoral Training Fellowship

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BOREDOM, PAIN AND ILLICIT DRUG USE IN MMT PATIENTS.

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Aims: To determine the extent to which use of illicit substances among patients in methadone maintained treatment (MMT) is predicted by levels of reported pain, boredom, methadone dose, satisfaction with dose, depression and anxiety.
Methods: 142 MMT subjects were recruited from programs at Beth Israel Medical Center in Manhattan and Interfaith Hospital in Brooklyn and assessed with the Brief Pain Inventory (BPI) and Memorial Pain Assessment Card (MPAC), the Addiction Severity Index Lite, the Brief Symptom Inventory (BSI), the Barratt's Impulsiveness Scale (BIS) and the State Boredom Measure (SBM).
Results: Duration of time spent bored in the past 3 months was significantly correlated with levels of BPI Pain Interference (r=.23, p =.008) and remained so even after controlling for methadone dose, degree "held" by dose or freedom from drug cravings, BSI depression, BSI somatization, BSI anxiety, and BIS impulsiveness (r = .20, p=.03). To find the variables that would best predict the number of methadone only urine analysis (UA) results in the last 12 months, a stepwise linear regression was preformed with the following predictor variables: methadone dose, degree "held", anxiety, depression, and somatization scores from the BSI, sum scores from the BPI and MPAC, and item scores from the SBM. The best predictor of methadone only UA was the combination of the duration of time spent being bored and the degree to which patients reported being "held" by their dose, F (2, 123) = 8.23, p< .001. This explained 12% of the variance in methadone only UA in the last 12 months (R-squared = .118).
Conclusions: The results suggest that even in the context of low levels of reported pain, depression and anxiety, sustained boredom is an important marker for continued illicit drug use in MMT patients, and especially among those who are dissatisfied with their methadone dose. These results also suggest a never before studied link between boredom and pain that is worthy of further study.
Financial Support: Baron Edmond De Rothschild Chemical Dependency

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REDUCED HIPPOCAMPAL VOLUMES IN REGULAR CANNABIS USERS.

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Aims: Cannabis is the most commonly used illicit drug worldwide, but its effect on the human brain is unclear. Animal studies have shown that cannabis can have neurotoxic effects on the hippocampus, a brain region that is high in cannabinoid receptors. Evidence in human regular cannabis users (CB) is inconsistent. We examined hippocampal volumes (HPVs) in CB as compared to non-cannabis using controls (HC), predicting reduced HPV in CB versus HC, in association with greater severity of use.
Methods: We recruited 52 (25 males) CB and 31 (14 males) age, gender and alcohol use-matched HC. Details on frequency (M= 25 days/month), duration (M=16.9 years) and age of initiation (M=17 yrs) of regular use, and lifetime cumulative dose of exposure (M=78439 cones) were obtained. Brain images were obtained with a 3-T scanner. HPVs were traced using a validated protocol with the software ANALYZE 11 (Mayo) by the same investigator (VL). We conducted repeated measures analyses of covariance (ANCOVA), with hemisphere as the within-subjects factor; group and gender as between-subjects factors; and current IQ and whole brain estimate as covariates. Correlational analyses examined relationships between HPVs and cannabis use measures, controlling for age where required.
Results: There was a significant effect of group (p=0.002) and gender (p=0.033), indicating bilateral smaller HPVs in CB and females. There was no effect of hemisphere (F= 0.476, p=0.492). There were no significant associations between various indices of cannabis use and HPV.
Conclusions: We found significantly smaller bilateral HPVs in CB compared to HC. To date, it is unclear whether the reported changes precede or are associated with cannabis use. Further analyses are being conducted on the effects of additional measures of cannabis use and compounds, as well as clinical measures on this sample.
Financial Support: The study was supported by a National Health and Medical Research Council (ID:459111).

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IMPULSIVITY, BIOFEEDBACK, AND SUBSTANCE ABUSE TREATMENT.

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Aims: Impulsivity has been linked to increased risk for substance abuse and poorer treatment outcome. However, our knowledge regarding whether impulsivity can be modified by treatment is limited. This study tests the hypotheses that A) treatment will improve behavioral but not personality measures of impulsivity and B) the addition of a biofeedback intervention will further improve behavioral impulsivity measures.
Methods: Adult patients enrolling in a daily outpatient substance abuse treatment program at Linden Oaks Hospital were recruited. Subjects (n=24) completed BIS-11, Balloon Analogue Risk Task (BART), and Stop Task upon enrollment and at the end of treatment. Treatment consisted of 3-5 hours per day of therapy including of 12-step facilitation, cognitive behavioral therapy, and motivational enhancement therapy, approximately 3 weeks in duration. Half of the subjects were randomly selected to receive biofeedback (BIO) treatment in addition to standard (STA) treatment. BIO treatment consists of 9 sessions of 20 minutes of relaxation and deep breathing with heart rate variability (HRV) feedback. Data collection is ongoing. ANOVA and paired t-tests were used with preliminary data to test for differences from pre- to post-treatment.
Results: For the 24 subjects completing the study so far, BIS total scores, and performances on the BART (adjusted pump average) and Stop Task (Stop-signal reaction time) did not change significantly with treatment, and was unaffected by biofeedback intervention. However, there was a non-significant decrease in each impulsivity measure for both groups combined.
Conclusions: Our findings thus far suggest that these measures of impulsivity are relatively stable characteristics that are not dramatically changed by short-term standard treatment or HRV biofeedback. Inclusion of additional participants may reveal whether treatment improves performance on these measures of impulsivity.
Financial Support: Linden Oaks Hospital; NIDA DA021336 (PI: A.A. Palmer) and DA02812 (PI: H. de Wit).

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HEALTH CONDITIONS, HEALTH STATUS AND SUBSTANCE USE SEVERITY AMONG ADULTS WHO USE METHAMPHETAMINE.

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Aims: Limited information is available on health outcomes among adults with long histories of methamphetamine (meth) use. This study examines factors associated with health status and rates of substance-related health conditions among meth users, with reference to national health statistics.
Methods: Data are from a 2009-10 long-term follow-up interview in an intensive natural history study of adults who had used meth regularly at recruitment in 1999-2003. Subjects (N=255) initiated use an average of 23 years prior to the follow-up interview, and 24% were using in the 30 days prior to the interview. Substance-related health conditions (e.g., hepatitis, STDs, injuries) and self-reported health status and disability were examined for younger (age 26-44) and older (45-64) subjects, and in relation to demographic factors and substance use severity. Data from the National Health Interview Survey (NHIS) are examined for comparison purposes.
Results: More than one-third (38%) of this sample reported having a major acute and/or chronic health condition that limited work and daily activities, including motor vehicle accidents, coronary disease and HIV. Substance use severity was related to health status, e.g., injection drug users (IDU) were more likely than non-IDU to report having had an STD (p<.05), hepatitis (p<.001) or cancer (p=.05), and were more likely to report having a disability (p<.01); younger adults (age 26-44) with dental problems reported using meth an average of 22 days compared to 18 days per month for those without dental problems (p<.01). Younger adults had a higher rate of hypertension (18%) compared to their counterparts in the NHIS sample (9%). One-third (34%) of younger adults in our sample reported fair/poor health whereas only 7% did so in the NHIS. Multivariate analyses further examine the relationship of health status, age and substance use severity.
Conclusions: These preliminary findings suggest linking primary care and substance abuse treatment may be particularly important for younger adults with a history of meth use.
Financial Support: NIDA DA025113

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ORAL THC DOES NOT BLOCK THE DISCRIMINATIVE STIMULUS EFFECTS OF MARIJUANA IN CANNABIS-DEPENDENT INDIVIDUALS.

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Aims: This ongoing study evaluates whether cannabis dependent individuals can be trained to discriminate between marijuana and placebo to validate drug discrimination as a model for assessing potential treatment medications for cannabis related disorders. In the absence of an effective medication, we are using a proof-of-concept approach to test whether oral THC blocks marijuana's discriminative stimulus effects.
Methods: Participants first are trained to discriminate marijuana (2.7% THC) from placebo (0.02% THC) cigarettes. Dose-response functions then are generated to determine whether varied THC concentrations (0.02, 1.7, 2.7%) occasion marijuana-appropriate responding (demonstrating pharmacological sensitivity). Next, different pretreatment doses of oral THC (0, 10, 20 mg) and a drug from a different class (d-amphetamine: 0, 5, 10 mg) are administered in combination with placebo (0.02% THC) marijuana to determine whether they occasion marijuana-appropriate responding (demonstrating pharmacological selectivity or substitution). Finally, participants are acutely pre-treated with oral THC (0, 10, 20 mg) prior to smoking a marijuana cigarette (0.02, 1.7, 2.7% THC), to examine whether oral THC alters the discriminative stimulus effects of marijuana. Subjective and physiological effects are monitored throughout each session.
Results: Of the 18 participants who began the study, 12 learned the discrimination. In the 8 completers thus far marijuana cigarette discrimination (2.7% vs. 0.02% THC) was reliable, and 1.7% THC occasioned marijuana-appropriate responding. Oral THC alone had subjective and physiological effects similar to those of smoked marijuana and both active oral THC doses substituted for marijuana.
Conclusions: Oral THC potentiated the subjective effects of marijuana, although under the 20 mg oral THC/2.7% marijuana cigarette condition the discriminative stimulus and a few subjective effects were attenuated albeit minimally.
Financial Support: Supported by NIDA R01 DA026761 and Joe Young, Sr. funds from the State of Michigan.

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THE ROLE OF DOPAMINE VS. GLUTAMATE SIGNALING IN THE NUCLEUS ACCUMBENS ON MOTIVATION FOR COCAINE: EFFECTS OF SEX AND STAGE OF ADDICTION.

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Aims: Evidence demonstrates sex and ovarian hormone modulation of dopaminergic (DAergic) signaling following initial cocaine exposure; however, very little information is available on sex differences at later stages of addiction (i.e., following chronic exposure) or on sex differences in glutamatergic signaling that may cause males and females to respond differently to cocaine. In this study we examined the contribution of DA versus glutamate signaling in the nucleus accumbens in motivation for cocaine in both males and females at an early versus a later stage of cocaine addiction (i.e., following short access (ShA) versus extended access (ExA) cocaine self-administration).
Methods: Male (N=24) and female (N=19) Sprague Dawley rats were trained to self-administer cocaine under a fixed ratio 1 schedule (1.5 mg/kg/infusion, 20 infusions maximum), and once acquired, they were given either ShA to cocaine consisting of 3 additional fixed ratio 1 sessions or ExA to cocaine consisting of 10 days of 24-hr access to cocaine under a discrete trial procedure (4 infusions/hr). Following 14 days of abstinence, motivation for cocaine was assessed under a progressive-ratio (PR) schedule, and once stable, the effects of intra-accumbens infusions of the D1 receptor antagonist SCH23390 (0-3.0 μg/side) or the AMPA/KA receptor antagonist CNQX (0-0.1 μg/side) were examined.
Results: Motivation to obtain cocaine was greater following ExA as compared to following ShA self-administration, particularly in females. Intra-accumbens infusion of SCH23390 dose-dependently decreased PR responding for cocaine after ShA but not after ExA cocaine self-administration; whereas, CNQX decreased PR responding for cocaine after ExA but not after ShA self-administration. Although the effects of CNQX did not seem to differ between males and females, females appeared to have an enhanced sensitivity to the effects of SCH23390.
Conclusions: These findings suggest that the contribution of dopamine versus glutamate signaling in cocaine addiction varies by sex and stage of addiction.
Financial Support: Supported by NIDA grant R01DA024716

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DIFFERENTIAL NEUROANATOMICAL CORRELATES OF ADOLESCENT AND ADULT METHAMPHETAMINE ABUSE.

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Aims: Preclinical evidence suggests that methamphetamine (MA) use may entail differential alterations in adolescent and in adult brain. However, in vivo brain changes in human adolescent MA abusers are not completely understood.
Methods: We analyzed high-resolution brain magnetic resonance images from 55 MA abusers (26 adolescents and 29 adults) and 58 matched controls (28 adolescents and 30 adults) using a surface-based approach.
Results: MA exposure was associated with thickness reduction in dorsolateral prefrontal cortices, most prominent in bilateral superior and left inferior frontal cortices (corrected $P<0.01$). MA-related thickness reductions in left insula and left superior temporal cortical regions were larger in adolescent than in adult MA abusers (P for interaction= 0.017 and P for interaction=.0.043, respectively). The interaction effect between MA exposure and age group was noted in left insula cortex (corrected $P<0.01$). Lifetime cumulative dosage of MA was associated with left prefrontal thickness deficits (left superior frontal cluster, r=-0.34, P=0.012; left inferior frontal cluster, r= -0.317, P=0.019). However, adolescent-specific insular thickness reduction was not correlated with any MA use measures.
Conclusions: Prolonged MA use was associated with cortical thinning in dorsolateral prefrontal regions which are especially vulnerable to the neurotoxic effects of MA, both in adolescent and adult MA abusers. Given the crucial role of the insula region in uncertain risk and reward processing particularly in adolescence when inhibitory control of prefrontal cortices are not yet fully developed, insular thickness reduction in adolescent MA abusers may predispose adolescents to MA abuse.
Financial Support: This study was supported in part by a grant from the NIDA (5R01 DA024070, Drs. Lyoo, and Renshaw).

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CHARACTERIZATION OF SMOKING MOTIVES BETWEEN AFRICAN-AMERICAN AND EUROPEAN-AMERICAN SMOKERS.

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Aims: The primary objective of this study was to assess the racial difference in nicotine dependence (ND) and smoking motives assessed by Wisconsin Inventory of Smoking Dependence Motives (WISDM) between AA and EA smokers.
Methods: A total of 3,364 adult smokers (2,200 AA and 1,164 EA smokers) were included in the study, selected from the Mid-South Tobacco Family and case-control genetic studies.
Results: The average age was similar between AA (42.9±12.1) and EA smokers (42.3±12.2) and they started regular smoking at similar age (17.9±4.2 vs. 16.8±4.0). Females accounted for about 55% for both groups. AA smokers were less likely to have post high-school education (16% vs. 23%). On average, AAs smoked two less cigarettes per day (CPD) than EA smokers (25.1±10.3 vs. 27.2±9.6, $p<0.0001$), with similar FTND scores (7.5±2.1 vs. 7.2±2.2; $p=0.052$). However, there existed significant differences in the individual FTND items and 8 of 11 Brief WISDM subscales between the two groups. Particularly, 78% of AAs and 67% of EAs smoked their first cigarettes within the first 5 minutes of awakening. Considering that the time to the first cigarettes (TTFC) is suggested to be the best predictor of relapse, we investigated the racial difference in the likelihood of TTFC within 5 minutes after wake up and its relationship with CPD in the logistic regression. Compared with EAs, AAs are about 2.5 times as likely to smoke within the first 5 minutes (OR=2.53; 95% CI: (1.87, 2.79); $p<0.0001$). Across race, the odds of smoking within 5 minutes was increased 2.9 fold for every additional 10 cigarettes smoked (95% CI: 2.58, 3.21; $p<0.0001$). The racial differences remained significant even after adjusting for 11 Brief WISDM subscales.
Conclusions: We conclude that significant differences exist between AA and EA smokers in ND and smoking motives, and these differences may underlie the racial difference in the genetic makeup of ND.
Financial Support: This project was in part supported by NIH grant DA-12844.

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DCM OF WORKING MEMORY SYSTEM IN COCAINE DEPENDENCE.

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Aims: Cocaine dependence (CD) is associated with impairments in working memory (WM). Modern models propose to interpret the neural basis of WM as interactions between brain regions. It is still unclear whether there are alterations in effective connectivity within the WM system of CD subjects. Here we aim to answer this question.
Methods: Functional magnetic resonance imaging (fMRI) data were acquired from 19 CD and 14 matched control (NC) subjects while they performed a WM task with 2 levels of memory delay and 3 levels of digit load. Dynamic Causal Modeling (DCM10) in Statistical Parametric Mapping (SPM8) was used to measure effective connectivity. 7 regions of interest (ROIs), i.e., bilateral middle frontal gyrus (MFG), posterior parietal cortex (PPC), inferior frontal cortex, and right (R) anterior cingulate cortex, were used for DCM analyses, based on SPM activation analysis. In all DCMs, it was modeled that (a) each ROI connected to all other ROIs; (b) memory delay worked as driving inputs; (c) digit load worked as modulator.
Results: Bayesian model selection indicated that (a) the driving inputs entered DCMs through R PPC for both CD and NC groups; (b) the 2 DCMs with the digit load modulating the connection from R PPC to left PPC and the connection from R PPC to R MFG were the optimal models for the CD and NC groups respectively. Independent of model structure, the Bayesian model averaging results showed clear differences in modulation effects of digit load between the CD and NC groups.
Conclusions: The preliminary results showed that (a) CD and NC groups had different optimal DCMs for the modulation effects of digit load; (b) the strength of the modulation effects may be different between groups. These results are consistent with different regional activations associated with WM previously observed in CD subjects relative to NC subjects.
Financial Support: Supported by a Peter F. McManus Charitable Trust Grant (LM and FGM) and NIDA Grants P50 DA009262 and K02 DA00403 (FGM).

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WEB-BASED SURVEY OF PSILOCYBIN-OCCASIONED MYSTICAL EXPERIENCE.

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Aims: The goal of this study was to characterize mystical-type experiences that occur during non-experimental self-administration of psilocybin using two questionnaires previously used to assess mystical-type phenomena during experimental, laboratory psilocybin sessions.
Methods: An anonymous web-based survey was administered over a two-month period using an online survey tool (www.surveymonkey.com). Individuals interested in psilocybin and spiritual or personally meaningful experience were recruited by web, email and word of mouth advertisement. Of the individuals who began the survey, 1602 (52%) completed the 30-min survey and met all inclusion criteria.
Participants completed the Mystical Experience Questionnaire (MEQ; 43 items) and the Hood Mysticism Scale (M Scale; 32 items) in reference to a single psilocybin session (period of drug action) during which they had a mystical or otherwise profound and personally meaningful experience. The majority of participants (80%) provided a narrative description of their session.
Results: Participants (18-83 years; 50% female) represented a wide range of income and education levels, countries of origin, and lifetime hallucinogen use. Most participants self-identified as 'spiritual but not religious' (70%), had used psilocybin more than 5 times (70%), were relatively young at the time of their psilocybin session (M = 25, range = 18-70), and endorsed having had a mystical experience during their session (88%). More than half considered their psilocybin session among the five most personally meaningful (51%) and spiritually significant (62%) experiences of their lives. Participants who judged the session to be mystical (compared to those who did not) had significantly ($p < .001$) higher scores on the M Scale (M = 230 vs. 184) and the MEQ (M = .69 vs. .50).
Conclusions: Results demonstrate that psilocybin can occasion personally meaningful and spiritually significant mystical experiences under varied conditions outside the laboratory, suggesting the external validity of double-blind studies of mystical-type effects of psilocybin.
Financial Support: DA03889; Council on Spiritual Practices

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METHAMPHETAMINE PRODUCES CONTRASTING EFFECTS IN NEURODEVELOPMENTAL GENE EXPRESSION IN ADOLESCENT AND ADULT MICE: RELEVANCE TO ADOLESCENT ADDICTION?

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Aims: The adolescent brain is particularly susceptible to addiction, as early onset of drug use results in much higher prevalence of addiction to alcohol, nicotine, methamphetamine, cocaine, opioids and other drugs. Methamphetamine (METH) is a major public health challenge as METH use increased by 60% in 2009, METH users display a rapid transition to iv use, and METH addiction in youth is increasing. To clarify the heightened susceptibility of youth to METH addiction, we hypothesize that METH affects normal neurodevelopment by altering axonal guidance molecules (AGMs) differently in adolescent and adult brain. AGMs are critical for neurodevelopment, neurogenesis and neuroadaptation.
Methods: We compared METH (5 mg/kg) with saline in 12 adolescent male (30 days) and 12 adult male mice (10 weeks), given i.p. daily for 6 days, by measuring locomotor activity, stereotypy and mRNA expression of AGMs in 3 brain regions.
Results: METH (5 mg/kg) increased locomotor in adolescent and adult mice, but in the adolescent mice: (1) peak effects were later; (2) locomotion was higher; (3) duration was longer. In the two age cohorts, specific AGMs and dopamine receptors differed following METH treatment in hippocampus (e.g. ephrin A3), in striatum, (e.g. neuropilin-1) and in cerebellum (D5 dopamine receptors).
Conclusions: METH produces different effects on locomotion and AGM gene expression in adolescent and adult mice. Altered mRNA expression levels of specific AGMs in hippocampus, striatum and cerebellum conceivably are associated with the cascade of METH-induced neurodevelopmental, morphological, behavioral, cognitive changes in hippocampus and other brain regions. Combined with other strategies, this novel approach may clarify the role of AGMs in mediating heightened susceptibility of the adolescent to the adverse consequences of METH and similar psychostimulant drugs of abuse.
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FACTORS ASSOCIATED WITH MEDICATION ADHERENCE AMONG PSYCHIATRIC OUTPATIENTS WITH SUBSTANCE ABUSE HISTORIES.

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Aims: To determine the extent of and factors associated with psychiatric medication non-adherence among a sample of psychiatric outpatients with a high rate of substance abuse.
Methods: Consecutive new admissions to an urban continuing psychiatric day treatment program were recruited during 2003-2005. The analysis involves patients who were prescribed psychiatric medication from different providers during the prior six months (N=131). Confidential research interviews were conducted at admission that included a modified Medication Adherence Rating Scale (MARS). All results are significant at $p<.05$.
Results: Age (mean) 39 y; male 61%; Hispanic 60%; Black 36%; White 18%; public assistance/disability 73%; DSM-IV diagnoses: major depression 26%, schizoaffective 21%, bipolar 16%, schizophrenia 13%, other 24%; substance abuse history 93%; drug/alcohol abuse within past 90 days 74%. A mean of 3.3 non-adherence items were endorsed on an 8-item MARS. Factors related to lower adherence scores were: lower satisfaction with medication, lower friends' support for drug/alcohol abstinence, higher engagement in processes of change, more medication side effects, lower self-efficacy for drug avoidance and lower social support for recovery. In multivariate regression analysis, only the last three factors remained significantly associated with non-adherence. In addition,one-third said their psychiatrists did not spend enough time with them to explain side effects or were rushed,
Conclusions: Low medication adherence was associated with side effects, a cognitive factor and a social factor. This suggests that technical aids may be insufficient since low adherence is not attributable to simply forgetting to take medication. Strengthening adherence should also include better education about side effects and the importance of adherence to sustain the benefits of medication. Psychiatrists should also be encouraged to address patients' adherence strategies, since the time devoted to addressing that during treatment may prevent serious adverse events such as relapse, treatment drop-out and hospitalization.
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LIFETIME STRESS IS ASSOCIATED WITH INCREASED DAILY USE OF COCAINE AND NICOTINE, AND ELEVATED ASI AND BDI SCORES, IN COCAINE-DEPENDENT PARTICIPANTS.

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Aims: The goal of this project is to evaluate the relationship between lifetime stress, addiction severity, and specific drug use variables.
Methods: Participants answered questionnaires, including the Lifetime Stress Checklist (LSC), Addiction Severity Index (ASI), Beck Depression Inventory (BDI), and Demographic/Drug use assessments.
Results: The sample primarily includes cocaine-dependent primarily African-American males (N=145, to date), who are 43.2±7.8 (mean ± S.D.) years of age. Volunteers reported using cocaine for 16.7±8.4 years and 19.2±8.8 days out of the last 30 days, and on average used 2.3±3.1 grams of cocaine/day. A majority were cigarette smokers (84%), who had been using nicotine for 21.5±10.3 years and were currently smoking 13.3±13.7 cigarettes/day. Using the LSC, participants were separated into those with high lifetime stress (HIStress; 11.6±3.6) or low lifetime stress (LOStress; 5.3±1.5) scores based on median split ($F1,144=196.225$, $p<0.0001$). ANOVA revealed significantly higher ASI scores for HIStress (1.4±0.6) vs. LOStress (1.2±0.5) groups ($F1,143=4.830$, $p=0.0296$), and significantly higher BDI scores for HIStress (15.3±9.5) vs. LOStress (9.5±8.3) groups ($F1,144=15.620$, $p=0.0001$). As compared to LOStress (11.4±11.3), those in the HIStress (15.2±15.6) group tended to smoked more cigarettes per day ($F1,132=2.624$, $p=0.1076$). Similarly, as compared to LOStress (2.0±1.9), the HIStress (2.7±3.9) group tended to consume more grams of cocaine per day ($F1,128=2.161$, $p=0.1440$).
Conclusions: The results indicate that those with higher lifetime stress exhibited elevated BDI and ASI scores. In addition, those with higher lifetime stress exhibited trends of increased daily cigarette smoking and cocaine use. Data acquisition is continuing and outcomes for methamphetamine-dependent individuals will also be presented at the conference.
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MODAFINIL: A CONTROLLED TRIAL FOR COCAINE DEPENDENCE.

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Aims: To study the efficacy and safety of modafinil in cocaine-dependent outpatients.
Methods: Three hundred twenty-six potential subjects were screened, 130 subjects were randomized to placebo (PBO), modafinil 200 mg, or modafinil 400 mg for 8 weeks. One hundred twenty-three subjects comprised the intent-to-treat sample. Subjects received cognitive-behavioral therapy weekly. Subjects had quantitative urine drug screens three times weekly. Visual analog scales, adverse events were collected weekly. Serum modafinil levels were collected at Week 4 and Week 8. Percent new-use days, number of confirmed non-use days, weekly log transformed quantitative benzoylecgonine levels. Number of subjects in each group with three continuous weeks of abstinence was analyzed.
Results: Subjects randomized to the three groups did not differ. In the primary intent-to-treat analysis, modafinil was not superior to PBO in confirmed non-use days, new-use days, or quantitative log benzoylecgonine levels. There was a trend favoring the 400 mg group with three continuous weeks of abstinence (X2=4.41, df=2, p=0.11). The Brief Substance Abuse Craving Scale (BSCS) indicated superiority for 400 mg of modafinil in terms of reduced craving (Wald X2 group effect=7.4, df=2, p=0.025). Visual analog scales indicated superiority for both 200 mg and 400 mg for lower desire, high and likeliness to use. Analysis of outcomes in relation to modafinil levels is underway. Side effects were generally mild.
Conclusions: On all major primary analyses, modafinil was not superior to PBO in terms of confirmed non-use days, new-use days, or quantitative log benzoylecgonine levels. There was a trend favoring the 400 mg group on the number of subjects with three continuous weeks of abstinence. Self-report measures showed significant effects in favor of modafinil over PBO. In the present sample, Modafinil did not improve objective measures of treatment outcome.
Financial Support: This work was supported by NIH/NIDA, R01 DA016368.

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ADULT ADHD DIAGNOSIS ACCURACY IN SUBSTANCE USE DISORDER CLIENTS.

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Aims: Introduction: Attention Deficit/Hyperactivity Disorder (ADHD) is over-represented among adult patients with substance use disorders (SUD) in North-American population. However, in Europe, little is known about ADHD diagnoses in SUD samples. Most available European studies use screening tools whose accuracy in this specific patient population remains unclear. A reliable screening procedure would be most helpful in the development of adequate treatment services.
Objective: To compare ADHD screening and diagnostic tools in SUD sample. Our sample consisted in substance-dependent subjects seeking treatment in a specialist outpatient care centre in France (Aquitaine).
Methods: Within an ongoing open cohort study of patients seeking treatment for one or more substance addictions individuals were assessed for Adult ADHD with both screening (ASRS) and diagnostic instruments (MINI-Plus and CAADID). Both DSM-IV and DSM-V criteria were considered for the CAADID. Kappa coefficients were used to measure concordance between diagnostic and screening tools.
Results: 223 subjects were included in the study. The main problem substances were cannabis, tobacco, alcohol and opiates. 39% screened positive for adult ADHD (ASRS), 5% met DSM-IV criteria for adult ADHD using MINI-Plus, and 14% (14/97) met DSM-IV criteria for adult ADHD using the CAADID. Concordance between each classification methods was very low, ranged from 0.11 to 0.29. By using proposed DSM-V criteria with the CAADID, the prevalence of adult ADHD was 26% (25/97).
Conclusions: Prevalence rate of adult ADHD was high among SUD patients but depended on the tool used for ADHD assessment. The diagnosis accuracy may be improved by lowering the cut-off as proposed by DSM-V revision group.
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BENZODIAZEPINE USE IN METHADONE MAINTENANCE TREATMENT PATIENTS.

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Aims: Benzodiazepine use is prevalent among methadone maintenance treatment patients and is a significant clinical phenomenon that is not well understood. We hypothesized that most patients using benzodiazepines in methadone maintenance treatment were self-medicating anxiety symptoms and would report having limited access to treatment.
Methods: Participants were recruited from a single methadone maintenance clinic by offering benzodiazepine-using patients $25 to participate in a research interview.
Results: The recruited sample (n=36) was mostly male (61.1%), white (47.2%), unmarried (55.6%), and unemployed (44.4%). Participants reported recently obtaining benzodiazepines from prescription (33.3%), illicit sources (36.1%), or both (30.6%). The lifetime pattern of obtaining benzodiazepines was prescription only (13.9%), illicit source only (16.7%), and both illicit and prescription (69.4%). The mean duration of benzodiazepine use was 65.3 (SD 73.6) months and mean length of methadone treatment was 20.7 (SD 35.4) months. Alprazolam was the most favored benzodiazepine (69.4%), followed by clonazepam (19.4%), and diazepam (11.1%). Most participants (58.3%) reported initiating benzodiazepine use prior to beginning methadone maintenance treatment. The most common reason for benzodiazepine use was treating symptoms of anxiety (33.3%), followed by prevention of benzodiazepine withdrawal (19.4%). Most participants (55.6%) were satisfied with their methadone dose and 36.1% thought their dose was too low. A minority (25%) of participants were receiving psychiatric care, although 51.6% reported it would be "very easy" to obtain psychiatric care. Most participants (80%) reported they wanted to stop using benzodiazepines.
Conclusions: Benzodiazepines used by methadone maintenance patients are from a combination of prescribed and nonprescribed sources. Most users would like to discontinue but are not under medical supervision for doing so. Treatment access does not appear to be an important factor.
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D-AMPHETAMINE WITHDRAWAL PARADIGM IN METHAMPHETAMINE DEPENDENCE.

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Aims: Treatment-seeking methamphetamine(METH)dependent individuals were enrolled in a 4-wk, double-blind, placebo-controlled, trial examining the impact of abruptly terminating oral d-amphetamine(DEX) administration in METH dependent humans on withdrawal, sleep, and cognition.
Methods: Participants were admitted to a residential facility, inducted onto DEX during week 1, randomized by severity of METH dependence, sex, METH Withdrawal Assessment (MAWA) score and history of ADHD to receive DEX or placebo (PLA) during wks 2-3. All participants received PLA during wk 4. Participants received standard treatment for substance abuse. Assessments (vitals, mood, cognitive performance, withdrawal/craving scores, sleep measures) were completed at least weekly.
Results: 14 METH-dependent volunteers(6 male,all Cauc,mean age 35.6 yrs) completed at least 2 wks of the study. Baseline characteristics did not differ between grps, except age (DEX=39.1±6.7, PLA=32.0±5.0;p=0.04). Preliminary analyses indicate "desire for METH" mean scores differed at the end of week 2 (DEX=1.0±1.7,PLA=10.7±10.7;t=-2.52,p=0.04) and a trend toward significant time (t=-2.2,p=0.06) and grp time interaction (t=1.97,p=0.09). MAWA score (t=-2.13,p=0.07) and METH Selective Severity Assessment(MSSA) score (t=-2.10,p=0.07) also showed a trend toward a difference between grps at the end of week 2. There were also trends toward time x grp interaction for MAWA (t=2.24,p=0.06), MSSA (t=2.08,p=0.08) and sleep quality (t=-2.00, p=0.09) ratings. Though there were significant decreases in supine (t=2.88,p=0.02), seated (t=3.19,p=0.02) and standing (t=3.25,p=0.01) HR between wks 1 and 2 in the PLA grp, no significant changes in HR were found in the DEX grp.
Conclusions: To our knowledge, this is the first double blind, PLA-controlled trial measuring pharmacologic effects of abruptly stopping amphetamine in METH dependent humans. Preliminary results suggest this amphetamine withdrawal paradigm may be useful in examining the efficacy of pharmacologic agents in alleviating early METH withdrawal symptoms.
Financial Support: Supported by NCRR grant RR020146

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SEX DIFFERENCES IN PATIENTS WITH CHRONIC PAIN AND PRESCRIPTION OPIOID ABUSE DURING BUPRENORPHINE/NALOXONE MAINTENANCE.

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Aims: Prior studies examining sex differences in prescription opioid dependence have found that women exhibit more psychiatric co-morbidity than men, while men demonstrate more aberrant drug use behaviors than women. To determine if there were similar findings in a sample of patients with chronic pain and opioid abuse, an interim analysis of sex differences was conducted.
Methods: 22 patients (13M, 9W) completed a 7-week inpatient and 3-month outpatient study investigating the abuse liability of prescription opioids under different doses of buprenorphine/naloxone maintenance (bup/nx).
Results: There were no significant baseline sex differences in ethnicity, age, type of pain, or years of prescription opioid use. The sample was primarily black (41%) or hispanic (36%), with an average age of 49 (±7) years. The majority had musculoskeletal pain (86%). Patients had used prescription opioids for approximately 11 (±16) years. Baseline rates of psychiatric co-morbidity did not differ significantly: 53% of men had an Axis I mood disorder, compared to 77% of women. Number of aberrant drug-related behaviors decreased for both groups across the 18-week study (M: 4.25 to 0.27; W: 4.0 to 0.5), as did the Hamilton-Depression-21 scores (M: 15.6 to 7.4; W: 15.3 to 11.1). Ratings (1-10) of average and worst pain over the past 7-days decreased in both sexes. For men, average pain decreased from 6 to 2.7, and worst pain from 8.5 to 4.8 (both ps <.05). For women, average pain decreased from 6.6 to 4.5, and worst pain from 9.1 to 6.5 (both ps <.05). Average bup/nx dose was slightly higher for women (M=18 mg, W=23.5 mg; p<.10). Urine toxicologies revealed little illicit opioid use throughout the study.
Conclusions: These data reveal that both men and women experienced an improvement in pain and depression, and had low levels of illicit opioid use during a 3-month course of outpatient bup/nx maintenance. There were no significant sex differences in pain relief, psychiatric co-morbidity or aberrant drug use behaviors.
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MOTIVATIONAL INTERVIEWING: A REVIEW OF CODING SYSTEMS.

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Aims: As the field of substance use continues to focus on the dissemination and implementation of evidence-based practice, questions arise on the most efficient and efficacious ways of training providers in evidence-based treatments. Training in motivational interviewing (MI) has been a particular focus among researchers, presumably because of its evidence-base among a variety of health behaviors. The evaluation of MI sessions using behavioral coding systems has increased substantially in recent years. Coding systems are used for a variety of purposes: to measure treatment fidelity to MI principles, to examine the mechanisms of change in treatment sessions, and to better understand the unique contributions of therapist and client language in session. As such, there are a number of coding systems available to researchers and clinicians.
Methods: Behavioral coding systems and systematic measures of MI treatment fidelity were identified from a recent review article and via a literature search using Medline and Psychinfo databases.
Results: Eight unique coding systems were identified and included in the current review. These coding systems include: 1) Behaviour Change Counselling Index (BECCI); 2) Helpful Responses Questionnaire, 3) Independent Tape Rating System (ITRS), 4) Motivational Interviewing Process Code, 5) Motivational Interviewing Skills Code (MISC), 6) Motivational Interviewing Supervision and Training Scale (MISTS), 7) Motivational Interviewing Treatment Integrity (MITI), and 8) Sequential Code for Observing Process Exchange (SCOPE). We will present descriptive and psychometric properties for each of the coding systems.
Conclusions: In response to the demand for further testing and implementation of evidence-based treatments, several measures of MI competence have emerged. These coding systems vary in their extensiveness and in the level of detail provided. Recommendations for use of the available coding systems and for future development of coding system will be discussed.
Financial Support: NIDA Grants (T32 DA007250, R21DA025135, and R01DA021227)

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IMPULSIVITY ANALYSIS BETWEEN SUBSTANCE DEPENDENCE AND SUGAR DEPENDENCE SUBJECTS.

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Aims: Many studies have confirmed a strong association between impulsivity and addictive behaviors. The aim of this study was to compare the impulsivity between sugar dependence and psychoactive substance dependence subjects.
Methods: A convenience sample of 803 individuals (48% female, mean age 34±12yrs, 11% obese) responded to a questionnaire on sugar and other psychoactive substances dependence based on DSM-IV criteria for substance dependence, fagerström test for nicotine dependence and Barratt Impulsiveness Scale (Bis-11) for impulsivity. Data were collected in two Brazilian state capitals and they were analyzed by the Chi-square test.
Results: Overall, 45% of the sample had a diagnosis of substance dependence (16% marijuana, 14% cocaine, 27% alcohol and 31% nicotine) and 37% sugar dependence. After bivariate analyses, subjects with substance dependence had higher level of impulsivity than non-substance dependence (47% vs. 23%; p<0.001). The analyses for each substance dependence showed the same results (marijuana - 61% vs. 28% - p<0.001; cocaine 65% vs. 28% - p<0.001; alcohol – 55% vs. 25% - p<0.001; and nicotine - 48% vs. 27% - p<0.001). The same phenomenon of higher impulsivity could be observed between individuals with sugar dependence and non sugar dependence (46% vs. 26%; p<0.001).
Conclusions: This study suggests that subjects with substance dependence or sugar dependence exhibit more impulsivity than non-dependence subjects. This similarity is an important result to test the hypothesis of sugar addiction.
Financial Support: CNPq; FAPEMIG

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EXTENDED-RELEASE MIXED AMPHETAMINE SALTS AND TOPIRAMATE INCREASE ABSTINENCE RATES IN COCAINE-DEPENDENT INDIVIDUALS.

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Aims: Dextroamphetamine and topiramate are promising candidate medications for the treatment of cocaine dependence, and these medications are hypothesized to affect cocaine use via different mechanisms of action. We hypothesized that the combination of these two agents may lead to additive or synergistic effects.
Methods: A 12-week clinical trial compared extended–release mixed amphetamine salts (MAS) combined with topiramate to placebo for the treatment of cocaine dependence. The primary outcome was the achievement of three consecutive weeks of abstinence, assessed by urine toxicology and confirmed using self-report. Rates of abstinence were analyzed using logistic regression and retention was analyzed using Kaplan-Meier curves and log-rank statistics.
Results: Eighty-one participants were randomized to placebo (52%) or MAS-topiramate (48%), and were mostly male with a mean age of 42 years. Baseline characteristics were not significantly different between treatment groups. There was a significant main effect of treatment (P=.03), with 45% of MAS-topiramate group and 20% of the placebo group achieving three consecutive weeks of abstinence. A significant (α=.10) interaction effect between the level of baseline cocaine use and treatment (P=.06) was detected. The odds ratio of achieving three weeks of abstinence on MAS-topirate in the third tertile (highest baseline use) was 20 (95% CI: 1.41, 200) compared to placebo. The odds ratio in the first tertile (lowest baseline use) was not significant. Mean twelve-week retention rate was 72.6% but no treatment effect was observed (P=.99).
Conclusions: These results suggest that MAS-topiramate is an effective treatment for cocaine dependence and the effect is more pronounced in patients with higher baseline cocaine use.
Financial Support: NIDA grants: R01 DA022217, K23 DA21209, K24 DA022412
& K24 DA029647

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PSYCHIATRIST DECISION-MAKING TOWARDS PRESCRIBING BENZODIAZEPINES: THE DILEMMA WITH SUBSTANCE ABUSERS.

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Aims: Evaluate psychiatrists' decision making about benzodiazepine (BZD) prescribing.
Methods: We conducted an anonymous, internet-based survey of 25 outpatient psychiatrists in an academic-affiliated public mental health center, using a modified, previously developed, 45 item questionnaire exploring psychiatrists' beliefs about patient request for BZDs, reasons for prescribing or not prescribing BZDs, and factors that influence the dilemma in whether or not to prescribe a BZD. 19/25 completed the survey.
Results: Psychiatrists most commonly experienced requests for BZDs for conditions commonly treated with BZDs (92.6%); however, 65% also, at times, experienced requests for behaviors suspicious for abuse, including 'lost/missing prescriptions' and 'use of BZD by others'. In contrast, items such as 'low suspicion of abuse' or 'patient not motivated to try alternatives' were occasional or common additional reasons for prescribing BZDs for 45.1%. Reasons NOT to prescribe included treatment concerns such as no indication for use, alternatives available, and concern for side effects (67.1%). Patient characteristics such as 'history of abuse', 'unknown patient', and 'patient use of illicit substances' were occasional or common reasons for NOT prescribing (74.6%). Work-related system issues (such as lack of time, additional workload of negotiating alternatives) were never a reason for prescribing BZDs for 76.6%. The top five reasons the majority of our sample had a dilemma in choosing whether or not to prescribe a BZD were patient history of abuse, fear of initiation of dependence, concerns for the patient, diversion, and feeling manipulated by the patient. Time limitations were only a dilemma for 21%.
Conclusions: Psychiatrist self-reported dilemma and behavior in prescribing BZDs involves patient characteristics associated with a substance abusing population and less frequently reflected work systems issues.
Financial Support: None

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β-CARBOLINES FOUND IN CIGARETTE SMOKE SUPPRESS MONOAMINE METABOLISM IN MOUSE BRAIN.

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Aims: Cigarette smoke contains the β-carbolines, harmane and norharmane, which inhibit monoamine oxidase (MAO) in vitro. Here we determined the effects of harmane and norharmane administration on tissue levels of 3,4-dihydroxyphenylacetic acid (DOPAC) and 5-hydroxyindole acetic acid (5-HIAA) in mouse brain, as a means for assessing the effects of these compounds on MAO activity in vivo.
Methods: Male C57BL/6 mice were decapitated 30 min after receiving harmane (3-20 mg/kg, i.p.) or norharmane (3-20 mg/kg, i.p.), and 120 min after receiving the selective MAO A inhibitor clorgyline (0.3-3.0 mg/kg i.p.). Brain tissue was rapidly dissected and frozen at -80 degrees C. Cortical and striatal concentrations of dopamine, DOPAC, serotonin and 5-HIAA were quantified by HPLC-ECD.
Results: Harmane, norharmane and clorgyline produced dose-dependent decreases in cortical DOPAC, while only harmane and clorgyline decreased cortical 5-HIAA. All drugs decreased striatal DOPAC without significantly altering striatal 5-HIAA. Importantly, the effects of harmane closely resembled those produced by clorgyline, suggesting the involvement of MAO A inhibition.
Conclusions: The findings in mice are consistent with in vitro evidence that harmane and norharmane inhibit MAO, and harmane is more potent in this regard. Furthermore, our results support the proposal that these β-carbolines could contribute to MAO inhibition produced by cigarette smoke.
Financial Support: Generously supported by NIDA IRP.

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A RANDOMIZED, CONTROLLED TRIAL OF BUPRENORPHINE DOSING REGIMENS FOR OPIOID-DEPENDENT YOUTH.

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Aims: To evaluate the relative efficacy of a 63-day vs. 28-day opioid detoxification with buprenorphine among opioid-dependent youth
Methods: Opioid-dependent adolescents and young adults (n=53; ages 13-24 eligible) were randomly assigned to receive a double-blind buprenorphine (Suboxone)-assisted taper of either 28 or 63 days in duration (in a parallel groups design). Participants' starting dose was matched to their clinical need, and tapers were structured such that participants' duration of exposure to buprenorphine was the same for all participants within a given condition, despite their starting dose. All participants received a common behavioral treatment of behavior therapy sessions and voucher incentives contingent on opioid-negative urine samples.
Results: Youth in the 63-day buprenorphine taper were retained in treatment significantly longer than those in the 28-day taper ($F(3,49)=12.8$; $p<.0001$). Youth in the 63-day taper achieved a significantly greater percent of urine samples documented to be opioid negative throughout the 63-day treatment phase ($F(3,49) = 6.90$; $p<.001$) and a significantly greater number of days of continuous abstinence from opioids ($F(3,49) = 4.24$; $p=.01$). Multivariate regression analyses indicated that being homeless or an injection opioid user predicted worse treatment outcomes.
Conclusions: Results demonstrate that buprenorphine may be safe and efficacious in the treatment of opioid-dependent youth and that a slower buprenorphine taper produces significantly greater treatment outcomes for this population relative to a faster taper. As the prevalence of misuse of heroin and other opioids among youth has markedly increased in recent years (with some referring to these trends as an epidemic in the U.S.), and limited research has been conducted to identify efficacious models of treatment for this population, this research provides novel empirical data that can inform clinical practice in the treatment of this emerging and understudied cohort.
Financial Support: NIDA Grant #R01DA018297

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PSYCHOLOGICAL SYMPTOMS AND MODAFINIL EFFECTS ON SMOKING CESSATION.

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Aims: A Phase II Clinical Trial was conducted to examine the moderating effects of psychological symptoms on the efficacy of modafinil as a smoking cessation pharmacotherapy. It was hypothesized modafinil's effects would be enhanced in participants with elevated levels of symptoms known to be exacerbated by tobacco deprivation (e.g., depression, inattention and concerns with weight).
Methods: Subjects were treatment-seeking adults (18-55) who smoked 10 ≥ cigarette per day, had CO reading ≥ 10 ppm at intake, were medically stable, and were not receiving psychotropic medications. After completing a medical screen, subjects were randomly assigned to an active (300 mg) or placebo group. Assessments of self-reported smoking behaviors and psychological measures [Beck Depression Inventory (BDI), Conner's Adult ADHD Rating Scale (CAARS), and Weight Concerns Scale (WCS)] were collected at baseline. Pharmacotherapy continued for 8 weeks, and smoking status was assessed weekly through treatment and then 1 and 12 weeks post treatment. For this interim assessment of how psychological symptoms moderated the effects of modafinil on self-reported smoking behaviors, we fit generalized linear mixed models for Poisson-like responses.
Results: The CAARS subscales, BDI, and WCS interacted significantly with treatment (placebo versus modafinil); modafinil was more effective in those with lower scores across these measures. For example, the predicted smoking at 8 weeks would be 19.8 cigarettes per day on modafinil and 11.2 cigarettes per day on placebo for someone scoring 10 on the CAARS A (Inattention/Memory Problems) but would be 4.2 cigarettes per day on modafinil and 11.5 cigarettes per day on placebo for someone scoring 0 on CAARS A.
Conclusions: Contrary to the initial hypothesis, modafinil's efficacy as a smoking cessation aid was greatest among participants with lower levels of baseline symptoms that could be exacerbated by tobacco cessation.
Financial Support: R21DA023049, RR-15592, Cephalon

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SUBSTANCE ABUSE TREATMENT PARTICIPATION QUESTIONNAIRE FOR INCARCERATED ADOLESCENTS.

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Aims: In mandated treatment settings, it is often hard to gauge the degree of engagement in treatment, since indicators often used do not apply (no-shows, drop out, tardiness). The purpose of this study was to develop a series of questionnaires in which therapists and teens in such settings can rate degree of teen participation in substance abuse treatment (milieu and group-based).
Methods: To develop a pool of items, a literature review was conducted, and incarcerated teens were interviewed along with the professionals who work with them. A set of 30 items was generated and administered to a separate sample of teens (N=118) and their therapists. Over 80% of the sample had a substance use disorder. The average age was 17 years; 10% were girls; and 70% were non-white.
Results: Principal component analysis was conducted on teen and therapist versions of the questionnaire. Components extracted accounted for 33-55% of total variance. Internal reliabilities ranged from 0.77-0.92. Scales of positive and negative treatment engagement were found and significantly correlated as expected with criterion variables such as number of days used marijuana after release, unit behavior as rated by guards, and riskiness ratings of binge drinking ($p < 0.050$). Scale content reflected both overt behaviors (joking around, talking to others) and attitudes (interest in change).
Conclusions: Adolescent and therapist versions of this questionnaire may be useful in determining alcohol and drug treatment engagement for incarcerated teens. Cross validation in other samples and other confined settings is recommended.
Financial Support: Supported by R01 DA-13375

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ORX/HCRT NEURONS, WITHIN DIFFERENT SUBREGIONS OF THE HYPOTHALAMUS, ARE DIFFERENTIALLY RECRUITED BY CUES CONDITIONED TO COCAINE VS. NATURAL REWARD.

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Aims: Hypothalamic orexin/hypocretin (Orx/Hcrt) neural projections have been implicated in the regulation of feeding behavior and, more recently, as participating in the regulation of reward, particularly the conditioned effects of rewarding stimuli. We hypothesized that this neuropeptide system may be preferentially recruited and eventually dysregulated by cocaine. The aim of this study was to establish the recruitment pattern of Orx/Hcrt neurons induced by presentation of an SD conditioned to cocaine (COC) or a highly palatable conventional reinforcer, sweetened condensed milk (SCM) within different subregions of the hypothalamus: the lateral (LH) and dorsomedial (DMH) hypothalamus as well as the perifornical area (PFA).
Methods: Male Wistar rats were trained to associate a discriminative stimulus SD with the availability of cocaine or SCM (S+) versus saline or non-reward (S-). Following extinction of cocaine and SCM reinforced responding, rats were presented with the respective S+ or S- alone. The brains were dual-labeled for Fos and Orx/Hcrt in the LH, DMH and PFA.
Results: Presentation of the COC or SCM-associated SD after extinction stimuli elicited identical levels of reinstatement. Presentation of cocaine-predictive SD recruited a larger number of Orx/Hcrt cells in the LH and DMH than the SCM SD, SD predictive of non-reward, and extinction and naïve controls, as reflected by an increased ratio of Orx/Hcrt activated cells (i.e., % of Fos-positive Orx/Hcrt cells). In the PFA, the COC SD selectively recruited a larger number of Orx/Hcrt cells compared to the non-reward SD, extinction and naive controls. In the case of SCM, however, the non-reward SD and SCM SD produced the same pattern of Orx/Hcrt neural activation compared to extinction controls.
Conclusions: These findings support a differential role of the Orx/Hcrt system in compulsive-like cocaine-seeking vs. behavior motivated by conventional reward.
Financial Support: NIDA DA08467 and NIAAA AA018010 (FW)

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PET IMAGING OF DOPAMINE TRANSMISSION IN COCAINE DEPENDENCE PREDICTS RESPONSE TO TREATMENT.

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Aims: Positron Emission Tomography (PET) imaging studies have shown that cocaine dependence is associated with the dysregulation of striatal dopamine signaling, measured as low D2 receptor binding and low pre-synaptic dopamine release. Previous studies have also shown that these factors may be associated with cocaine seeking behavior. The goal of the present study was to investigate whether these factors were predictive of response to treatment.
Methods: All subjects underwent PET scans using [11C]raclopride: at baseline and after the administration of a stimulant (methylphenidate). These methods provide a measure of striatal D2/3 receptor binding (BPND) and dopamine release in response to a stimulant (deltaBPND). Following the scans, the cocaine dependent subjects were enrolled in 12 weeks of behavioral treatment using Contingency Management, where subjects earned voucher points for cocaine-negative urine samples.
Results: Response to treatment among the cocaine dependent subjects was measured as the amount of voucher money earned. The response to treatment among the cocaine dependent subjects was bimodal, and subjects were divided into two groups: treatment responders and non-responders. The PET outcome measures (BPND and delta BPND) were compared between these two groups in the limbic striatum. A significant difference was seen with both outcome measures, where BPND and delta BPND were lower in the treatment non-responders. This effect was greater with deltaBPND, a measure of pre-synaptic dopamine release.
Conclusions: These findings provide insight into the neurochemistry of treatment response and show that low dopamine transmission was associated with treatment failure.
Financial Support: National Institute on Drug Abuse

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MOOD/ANXIETY DISORDERS AND THEIR LONGITUDINAL ASSOCIATION WITH NON-MEDICAL PRESCRIPTION OPIOID USE AND PRESCRIPTION OPIOID USE DISORDER.

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Aims: Mood and anxiety disorders are highly associated with nonmedical prescription opioid use. We examined longitudinal associations between nonmedical prescription opioid use and opioid disorder due to nonmedical opioid use with mood/anxiety disorders in a national sample, examining evidence for precipitation, self-medication and general shared vulnerability pathways between disorders.
Methods: Data were drawn from face-to-face surveys of 34,653 adult participants in Waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. Logistic regression models tested for the hypothesized pathways.
Results: Baseline nonmedical prescription opioid use was associated with incident mood disorders (aOR:1.7[1.3-2.2]), anxiety disorders (aOR:1.4[1.1-1.8]), and generalized anxiety disorder (GAD, aOR:1.5[1.1-2.0]), baseline opioid disorder was not associated with any incident mood/anxiety disorders in wave 2, adjusted for baseline demographics, other substance use, comorbid mood/anxiety disorders, antisocial personality disorder (ASPD), and family history. Baseline mood disorders (aOR:1.5[1.2-1.8]), MDD (aOR:1.3[1.1-1.7]), and bipolar disorder (aOR:1.7[1.2-2.4]) were associated with incident nonmedical prescription opioid use at follow-up, adjusted for baseline demographics, comorbid mood/anxiety disorders, ASPD, other substance use, family history and pain. Baseline mood disorders (aOR:2.0[1.4-2.7]), MDD (aOR:1.6[1.1-2.4]), dysthymia (aOR:2.0[1.1-3.7]), and panic disorder (aOR:2.1[1.2-3.9]), were associated with incident opioid disorder at follow-up, adjusted for the same covariates.
Conclusions: Results suggest that preciptiation, self-medication as well as shared vulnerability are all viable pathways between nonmedical prescription opioid use and opioid disorder due to nonmedical opioid use with mood/anxiety disorders.
Financial Support: NIDA grants DA020667 & DA023434 (P.I. Martins).

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RECIPE FOR THC-LIKE ABUSE: JWH INDOLE-DERIVED CANNABINOIDS AND K2/SPICE.

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Aims: "Spice" blends, such as Spice Gold, Spice Diamond, and K2 are marketed as incense and have been sold over the internet since 2004 to users who smoke the mixtures for their cannabis-like effects. While the ingredient list for these blends contains only natural herbs, they have been found to contain cannabinoids, particularly indole-derived cannabinoids originally synthesized in Dr. John Huffman's lab. These "JWH compounds" are CB1 receptor agonists and produce cannabis-like effects. The present experiment marks one of the few studies to examine JWH compounds in vivo.
Methods: Fifteen JWH compounds were examined, all with a similar chemical structure to the JWH compounds found in Spice. Male ICR mice were injected with a dose of a JWH compound and assessed for spontaneous activity, tail flick analgesia, and rectal temperature (5-6 mice/dose). Effects were compared to those of THC.
Results: The majority of the compounds tested produced large locomotor decreases in the spontaneous activity test. Compounds also produced the maximum effect on the tail flick analgesia test, and produced decreases in body temperature. Therefore, the majority of the compounds tested produced pharmacological effects equivalent to those of THC, but the potency of the compounds varied widely. Compounds with higher CB1 affinity were more potent than those with lower affinity, and some were even more potent than THC.
Conclusions: These results suggest that these compounds collectively represent a class of cannabinoids with pharmacological effects that closely resemble those of THC and other psychoactive plant-derived cannabinoids. Based on these pharmacological effects, JWH compounds are likely to have as much abuse potential as THC. Due to the ease of obtaining these Spice blends, their popularity as legal drugs, and the lack of scientific knowledge about the safety in using such products, they remain a significant health concern in the U.S. and Europe.
Financial Support: NIDA grants DA-03590 and DA-03672

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ANTERIOR CINGULATE PROTON SPECTROSCOPY GLUTAMATE LEVELS DIFFER AS A FUNCTION OF SMOKING CESSATION OUTCOME.

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Aims: We previously reported that dorsal anterior cingulate cortex (dACC) functional connectivity was reduced in smokers who would 'slip' soon after beginning nicotine replacement therapy (NRT). Growing evidence suggests that dysfunctional glutamatergic neurotransmission is involved in mediating nicotine dependence. We hypothesized that pretreatment dACC glutamate levels would differ between smokers who slipped and remained abstinent during NRT.
Methods: Proton magnetic resonance spectra (MRS) were obtained from dACC and parieto-occipital cortex (POC) using two-dimensional J-resolved MRS at 4 Tesla and analyzed using LCModel. Nine nicotine-dependent women were scanned prior to making a quit attempt and grouped by NRT outcome (abstinence vs. slip: smoking ≥ 1 cigarette).
Results: Slip subjects (n=5) exhibited reduced dACC glutamate levels ($p<0.03$) compared to abstinent subjects (n=4). POC glutamate levels did not differ between groups. Additionally, slip subjects reported higher nicotine dependence scores (6.2 ± 1.3; $p<0.01$) compared to abstinent subjects (3.5 ± 1.3), but did not differ on any other demographic variable.
Conclusions: Dorsal ACC glutamate levels may be a useful biomarker for nicotine dependence and treatment outcomes. As the slip phenotype is a potential predictor for smoking relapse vulnerability, it is possible that reduced dACC glutamate levels may contribute to and be a biomarker for this phenotype.
Financial Support: This study was funded in part by National Institute of Health grants U01DA019378, R01DA022276, R01DA014764; R01DA09448; K02DA017324, T32DA015036, and S10RR13938; by funding from the Counter-Drug Technology Assessment Center (CTAC), an office within the Office of National Drug Control Policy (ONDCP) via Army Contracting Agency Contracts DABT63-99-C and DABK39-03-C-0075; and by research support from GlaxoSmithKline (GSK).

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DRUG MISUSE, VIOLENCE, AND HIV RISK AMONG YOUTH IN AN URBAN EMERGENCY DEPARTMENT.

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Aims: There is a critical need to understand drug misuse and associated risk factors (violence, HIV risk) among urban youth treated in the Emergency Department (ED). In particular, data is lacking among youth who present to the ED for a violent injury as compared to other youth in the ED.
Methods: Youth (14-24) presenting to an urban ED with a violent injury self administered a computer survey. A comparison group, matched by age and gender, was recruited. Validated screening questions included demographics, drug use, past partner violence, and weapon violence, alcohol, and sexual risk behaviors. A logistic regression analysis was used to predict drug misuse (NIDA- Modified ASSIST > 4) based on demographics, past violence, current reason for ED visit, and sexual risk behaviors.
Results: 804 youth were screened (85.2% participation rate). Overall, 42.2% presented with a violent injury, 54.2% were male, 63.1% were African-American, and 68.7% received public assistance. 40%(n=323) screened positive for misuse of one or more drugs (97.8% marijuana, 14.2% prescription sedatives, 13.0% prescription opioids, and 6.5% cocaine). Youth with drug misuse were more likely to be male (OR = 2.3, CI=1.6-3.3), not in school (OR = 0.7, CI=0.5-0.9), presenting with a violent injury (OR = 1.5, CI=1.1-2.0), and report partner violence (OR = 1.9, 1.2-2.4), multiple sexual partners (OR = 1.5, CI=1.0-2.1), and alcohol misuse (OR = 2.3, CI 1.6-3.3).
Conclusions: Youth seeking ED care for violent injury have high rates of drug misuse compared to a youth seeking ED care for other reasons. Youth screening positive for drug misuse were also likely to report exacerbated rates of partner violence and sexual risk behaviors. ED-based interventions for urban youth should address these multiple risk behaviors.
Financial Support: NIDA#024646

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A RANDOMIZED TRIAL EVALUATING THE EFFECTIVENESS OF A HEPATITIS CARE COORDINATION MODEL IN METHADONE MAINTENANCE TREATMENT.

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Aims: Evaluate a multi-component hepatitis care coordination intervention linking MMT patients to hepatitis services.
Methods: Participants were recruited from MMT programs in New York and San Francisco and randomized to:1)on site HIV and hepatitis (HAV/HBV/HCV) screening, counseling and education with motivational interviewing (MI), HAV/HBV vaccination, and 6 months of case management (CM) to promote adherence to HCV evaluation (HCC), or 2)on site HIV and hepatitis screening, counseling and education, and referral for off site HAV/HBV vaccination and HCV evaluation (TEC).
Results: Of the 489 participants, 299 needed HAV/HBV vaccine, 286 needed HCV evaluation, and 144 needed both. HCC participants were more likely to be vaccinated within 30 days (76% vs. 11%; $p < 0.001$). Logistic regression examining group differences in vaccination adherence (within 30 days) revealed a robust effect for HCC group (OR: 42.3; 95% CI: 19.5-91.9). HCC participants were more likely to attend an HCV evaluation during the CM period (53% vs. 33%; $p < 0.001$). Logistic regression examining adherence to HCV evaluation revealed a significant treatment group effect (OR: 2.3; 95% CI: 1.4-3.9). In a combined treatment outcome analysis (those only needing vaccine, only HCV evaluation, or both, within the study timeframe) 54% of HCC participants met the study goal compared to 16% of TEC. Logistic regression of the combined outcome showed a significant treatment effect (OR: 6.7; 95% CI: 4.3-10.5).
Conclusions: This study demonstrated that a comprehensive hepatitis care model, with on site vaccination, MI enhanced education and case management, integrated in MMT can significantly increase adherence to HAV/HBV vaccination and HCV evaluation, representing a viable strategy to address the HCV epidemic among drug users in MMT.
Financial Support: Supported by:NIDA Grants R01DA20781, R01DA020841, P30 DA011041, P50DA009253 & U10DA15815

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ESTROGEN ATTENUATES NOCICEPTIVE RESPONSES TO CARRAGEENAN-INDUCED INFLAMMATION IN A TIME-DEPENDENT MANNER.

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Aims: Estrogen dose-dependently produces antihyperalgesic effects in inflammatory models of hyperalgesia in rats. Elucidating the mechanisms by which estrogen affects inflammatory responses will greatly enhance our understanding of, and ability to treat, painful pathological conditions in the 8 million women receiving estrogen-alone hormone therapy. In this study, we aim to determine the time-course of estradiol effects on inflammatory-induced behavioral responses.
Methods: To this end, eight week old ovariectomized Sprague-Dawley female rats were subcutaneously implanted with Silastic capsules containing either 20% 17β-estradiol or cholesterol (vehicle). One week after surgery, behavioral testing was done. Paw withdrawal latencies (PWL) in response to a low (4.5mV), medium (4.9mV), and high (5.3mV) heat stimulus was measured using a Hargreaves PAW thermal stimulator prior to and at 1, 5, and 24 hours after injection of saline or carrageenan (1% injection into the intraplantar region of the right hind paw).
Results: Results reveal significantly dampened behavioral responses in animals that received the estradiol treatment compared to animals that received the vehicle treatment. Specifically, a significant interaction of time and hormone treatment was found at the low heat intensity in which the estradiol-treated 5-hour group had significantly longer PWL than the estradiol-treated baseline group, $F(1, 35) = 6.54$, $p < .05$. The 1-hour and 24-hour groups did not show significant interactions of time and hormone treatment, indicating that estrogen's anti-nociceptive effects are most potent in the 5-hour group.
Conclusions: Taken together, these data suggest that estrogen may be functioning to attenuate nociceptive responses in a time-dependent manner.
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SOCIAL AND ENVIRONMENTAL ENRICHMENT DIFFERENTIALLY ALTER MDMA-INDUCED LOCOMOTOR ACTIVITY IN MALE AND FEMALE ADOLESCENT RATS.

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Aims: Many factors influence the effects of drugs such as MDMA (ecstasy). Adolescence is a critical time during development when exposure to drugs of abuse is more likely to occur. The present study examined whether social and environmental factors alter MDMA-induced locomotor activity in adolescent male and female rats.
Methods: On postnatal day (PND) 23, rats were housed in one of several same-sex conditions. Both social (number of rats per cage) and environmental (availability of toys) factors were manipulated. Socially isolated rats were housed alone (1 rat/cage) in an environment that was either impoverished with no toys (II) or enriched with toys (IE). Other rats were housed in groups of three with (SE3) or without (SI3) toys. Starting on PND 30, 5 mg/kg MDMA was injected IP and MDMA-induced locomotor activity was measured for 30 minutes once daily for 5 consecutive days.
Results: In males, II rats had higher levels of exploration in response to saline than any other groups. On day 1, 5 mg/kg MDMA significantly increased activity only in male SE3 rats. However, over the 5 day period, behavioral sensitization to MDMA was apparent in all groups such that activity was significantly increased by the second day, except in male SE3 rats, which were not sensitized until day 4. In females, only SI3 rats exhibited significantly increased activity on day 1. All of the other groups of females became sensitized to MDMA and had significantly greater activity than saline animals by day 2 and this continued throughout the 5 day period.
Conclusions: These data show that the locomotor-stimulant effects of MDMA differ in males and females housed in different conditions. Further, there is an interaction between the social and physical environment in mediating the behavioral effects of MDMA in male and female adolescent rats. These data suggest that drug prevention and treatment strategies need to be specific to adolescent males or females, and need to take into account the different environments in which teenagers might live.
Financial Support: NIDA grant DA023996

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FACTORS ASSOCIATED WITH MENTAL HEALTH CLINICIANS' REFERRALS TO 12-STEP GROUPS.

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Aims: To investigate the relationship between clinicians' experience and attitudes and 12-step referral practices.
Methods: Staff (n=105) in 5 NYC mental health clinics completed a survey regarding their attitudes and 12-step referral practices. Attitude scales were adapted from the Positive/Negative Aspects of 12-step (PNS, Laudet, 2003), Clinician Optimism Scale (Grusky et al., 1989), and the Mental Health Confidence Scale (Carpinello et al., 2000). A new scale assessed clinician's assessment of the severity of substance abuse problems among clients currently on their caseload (α=.84). The dependent variable, referral practices, was measured with the Referral to Self-Help Practices Scale (Villano et al., 2005). Referral practices represented clinicians' beliefs and efforts that promoted clients' participation in 12-step groups. All measures were scored in the affirmative direction of the construct. Referral practices was regressed on attitude measures as well as on sociodemographics and separate measures representing interest in and experience with 12-step groups. Significance was $p<.05$.
Results: Mean years of clinical experience was 19 (SD=11.06); 67% reported having clients who were currently abusing drugs or alcohol; 43% reported attending a 12-step meeting for personal, and 39% for professional reasons. Referral practices was associated with greater interest in learning more about 12-step (β=.28) and favorable attitudes toward 12-step (PNS; β=.29). Interest in learning more about 12-step groups was associated with clients' problems with substance abuse (β=.48).
Conclusions: Efforts to integrate mental health and substance abuse services exist from the policy to the clinic level. However, mental health clinicians have not historically received training on managing clients with substance abuse problems, including encouraging such clients to attend 12-step groups. The results suggest that one method to increase mental health clinicians' readiness to promote 12-step is to generate interest in learning about 12-step by providing clinicians greater opportunity to work with substance abusing clients.
Financial Support: R01DA023119

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WITHDRAWN

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PERCEPTIONS OF BENEFITS AND RISKS OF METHAMPHETAMINE USE.

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Aims: Aims: Methamphetamine abuse continues to be a problem, but there has been little recent research into the reasons for its use. This paper seeks to determine the attitudes of methamphetamine users towards the benefits and risks of methamphetamine use and the problems associated with use.
Methods: Methods: This is a survey of 154 patients newly admitted to residential treatment who participated in a structured survey using computer-assisted interviewing. Inclusion criteria were having used methamphetamine at least six times in the last six months. Statistical methods include t-tests, chi squares and correlations, with significance set at .05
Results: Results: Fifty-eight percent were female, 83% were White, 10% Hispanic, and average age was 32. Mean score on the Severity of Dependence Scale was 1.6 out of 3 and 67% had previously received a mental health diagnosis. Besides methamphetamine, the most frequently used drugs in the month prior to entering treatment were alcohol (61%), marijuana (60%), powder cocaine (38%), alprazolam (38%) and hydrocodone (36%). Routes of administration of methamphetamine included smoking (61%), injecting (50%), snorting (38%), swallowing (21%), and shelving/shafting (3%).
The five major benefits to using methamphetamine reported by the respondents included increased energy/to stay awake (63%), enhanced sexual experience (54%), weight loss (38%), to get high and have a good time (32%), and increased confidence (31%). The five greatest risks were addiction/dependence (77%), paranoia (40%), depression (40%), anxiety (37%), and legal/police problems (36%). Higher scores on the severity of dependence scale were positively correlated with risk of dependence (p=.0006) and risk of anxiety/panic (p=.049).
Conclusions: Conclusions: The attitudes towards the benefits and risks of methamphetamine use offer new insights into reasons for use, and their relationships with severity of dependence. The strong negative attitudes towards risk of addiction/dependence may reflect the severity of problems experienced by the respondents after having recently entered treatment.
Financial Support: NIDA R21 DA025029, Period 8/15/2009-7/31/2011.

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POLY-DRUG USE AND HEROIN DEPENDENCE IN MALAYSIA, 1968 TO 2010.

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Aims: To explore patterns of poly-drug use and ethnic differences in Malaysian heroin users.
Methods: Timelines drug use histories detailing age of first use of heroin and of misuse of other substances (cigarettes, marijuana, alcohol, benzodiazepines, amphetamine-type stimulants, buprenorphine) were recorded by a single psychiatrist from 423 patients (all male) enrolling in 3 clinical trials between 2003 and 2010; demographic data was recorded at screening by a research assistant. We evaluated cumulative proportions of study participants reporting initiation of each substance since 1968 and compared results for Malays (N=351) and non-Malays (N=72).
Results: Cigarette smoking, marijuana and heroin use accrued steadily from the mid-1960s to 2008, by which time all patients had initiated heroin, 99% had initiated cigarette smoking and 80% THC. The numbers initiating alcohol or benzodiazepine use rose more gradually during this period, leveling off at 50% and 45% of the cohort, respectively, by 2006. ATS abuse rose explosively from about 10% in 1999-2000 to 65% by 2008; buprenorphine abuse showed a similar explosive rise beginning in 2001 and increasing to 38% of the cohort by 2008. Onset of cigarette, heroin, alcohol, benzodiazepine and ATS abuse followed a similar time course among Malays and non-Malays, but lifetime THC and ATS abuse peaked at lower levels among non-Malays (43%, 50%, respectively) compared to Malays (90%, 67%, respectively; p<.01 for both comparisons).
Conclusions: The study findings document high prevalence of poly-drug abuse in this population, reflecting great vulnerability to initiating new drugs of abuse as they become available. Routine surveillance of drug use patterns among treatment-seeking heroin dependent individuals may help identify emerging drug problems early in their onset. Differences in patterns of poly-drug use between Malays and non-Malays suggest that peer group and social factors (and possibly genetic differences) may affect vulnerability.
Financial Support: NIDA 1R01DA14718, 2R01DA014718, K24DA000445

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CHARACTERISTICS ASSOCIATED WITH DIVERSION OF SCHEDULED PRESCRIPTION MEDICATIONS AMONG YOUNG ADOLESCENTS.

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Aims: To estimate the prevalence of diversion (e.g., trading, selling, giving away or loaning) of four classes of scheduled medications (pain, stimulant, anti-anxiety and sleeping) among young adolescents, and to identify characteristics of young adolescents who divert prescription medications.
Methods: A web-based survey was administered to a population-based sample of 2,597 secondary school students in 2009-2010. The sample was 51% female with a mean age of 14.8 years; 30% African-American, 65% White, 4% Asian, and 1% Hispanic.
Results: Approximately 13.8% (n = 117) of lifetime medical users of scheduled pain, stimulant, anti-anxiety and sleeping medications (n = 848) reported ever trading, selling, giving away or loaning their medications. The leading type of diversion was giving away or loaning (11.4%), followed by selling (4.8%), and trading (2.6%) prescription medications. Among past-year medical users, about 18.2% (n = 85) had diverted their medications. The odds of a positive screen for drug abuse among lifetime medical users who diverted their medications were more than twelve times greater than nonusers (AOR = 12.6, 95% CI = 7.7 – 20.6, p < .001), while the odds of a positive drug screen did not differ significantly between lifetime medical users who never diverted and nonusers. Multiple logistic regression analyses indicated being non-White, substance use, and other externalizing behaviors were significantly associated with diversion after adjusting for relevant covariates.
Conclusions: The findings indicate that a minority of young adolescents in our study area who are prescribed scheduled medications divert their own medications. Substance abuse and other externalizing behaviors are considerably more prevalent among adolescents who divert their prescription medications. Careful assessment, prescribing and monitoring could be useful in reducing the diversion of prescription medications among young adolescents.
Financial Support: This research was supported by R01 DA024678.

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INTERACTION OF ALCOHOL AND HIV.

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Aims: This study was undertaken to explore significant interactions that occur between alcohol and HIV and between alcohol and antiretroviral regimens that include either ritonavir or efavirenz based on their metabolic pathways.
Methods: Preliminary data is presented from a double-blind, placebo-controlled, randomized, within-subjects study in which individuals with HIV disease not currently receiving highly active antiretroviral therapy (HAART) participated in two study sessions in which they received either alcohol (1g/kg) or placebo. HAART was then initiated with observed dosing for two weeks. This was followed by repeated study sessions in which alcohol or placebo was administered with HAART. Pharmacokinetics, subjective, and cognitive responses were collected at baseline and over the 8h (alcohol alone) or 24h (alcohol + HAART) study sessions. Area under the curve (AUC) was calculated and examined by paired t-test. P<0.05 (two-tailed) was considered significant.
Results: Fourteen individuals (2 women) 7 Caucasian, 4 African-American, 3 Latino participated. Blood alcohol concentration (BAC) was significantly higher prior to HAART compared to after HAART (p=0.02). A trend for greater alcohol-associated "high" following HAART was observed (p=0.06).
Conclusions: Patients with untreated HIV disease demonstrate higher BAC compared to after receiving HAART. Higher BAC may be mediated by host response to HIV which is associated with immune activation and, possibly, damage to the intestinal mucosa mediated by the inflammatory response at the site of gut-associated lymphoid tissue. In untreated HIV disease, this may contribute to greater toxicity of alcohol. Greater subjective "high" in HAART-treated patients may be due to pharmacodynamic interactions between alcohol and efavirenz-containing regimens.
Financial Support: Supported by: NIAAA/NIH RO1 AA 018001 and K24 DA 023359

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MARIJUANA USE AMONG HIV PATIENTS.

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Aims: One qualifying condition for medical marijuana use is HIV/AIDS, yet little is known about the behavioral or health impacts of smoking marijuana (MJ) among patients with HIV/AIDS. To begin to address this issue, we examined prevalence, pattern and persistence of MJ use, other substance use, acute healthcare utilization, and correlations with demographic and behavioral characteristics in patients receiving integrated substance abuse treatment within a large urban HIV primary care clinic.
Methods: Standardized, self-reported survey data were collected prior to substance abuse treatment and 6 months following initiation, limited to patients reporting some substance use in the prior 30 days (excluding those transferring from controlled environments).
Results: Of 230 patients, more than half reported past 30-day MJ use (n=180) with 58.5% of the latter reporting >=15 days use. MJ users and nonusers did not differ in gender, race/ethnicity, living situation, employment, psychological symptoms, and use of alcohol, cocaine, or benzodiazepines. In bivariate analyses, MJ users were significantly younger (M= 38.5 vs 45.7 years); less likely to be on probation/parole (9.5% vs 19.8%); and, during the prior 30 days, less likely to use opiates illegally (5.9% vs 14.3%), less likely to use outpatient/emergency facilities for acute care (55.9% vs 70.5%), and less likely to use prescribed psychotropic medications (24.8% vs 40.2%) than nonusers. In multivariate analyses, only younger age and less healthcare use remained significantly related to MJ use. Treatment did not significantly alter MJ use 6 months later, but other substance use declined.
Conclusions: Marijuana use was common in these HIV patients, unaltered by treatment, and related to younger age and acute outpatient/emergency healthcare utilization. These data suggest several hypotheses for evaluation: healthier patients may self-select MJ use; MJ use be associated with consequences that create barriers to seeking healthcare; MJ use may have medicinal value that reduces need for such care.
Financial Support: Supported by SAMHSA/CSAT grant TI018711 and Joe Young, Sr. Funds (State of Michigan)

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SMOKING STEREOTYPY IS ASSOCIATED WITH DECREASED CAUDATE ACTIVATION DURING BEHAVIORAL CONTROL.

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Aims: Nicotine dependence (ND) is a multidimensional syndrome and smokers exhibit variability on ND factors including tolerance, drive, and preference for smoking over other reinforcers (Shiffman, Waters & Hickox, 2004). Whereas research has examined the validity of ND dimensions, little work has investigated potential neurocognitive correlates. In the current analyses we examined relations between one ND factor—'Stereotypy' or, the degree to which smoking is inflexible across situations and time—and brain activation during inhibition of prepotent responses on a Go/NoGo task. We hypothesized these variables would be correlated given both reflect behavioral control over a prepotent/overlearned response.
Methods: 33 adult smokers were fMRI scanned while completing a variant of the Go/NoGo task with three trial types (Chikazoe et al. 2007): frequent Go (75%), infrequent Go (12.5%) and Stop (12.5%); SOA = 800 ms. Using FSL, we modeled Behavioral Control (BC)-specific activation (Stop > Infrequent Go) and correlated this contrast with Stereotypy scores on the Nicotine Dependence Symptom Scale (NDSS; Shiffman, Waters & Hickox, 2004).
Results: Mean Stereotypy scores and task performance were comparable to those observed in previous studies. Across the sample, BC-specific activation was observed in striatum, insula, and temporal gyrus. Regression analyses revealed negative correlations between Stereotypy and BC-specific activation in dorsal striatum—a region involved in the habit learning, even after controlling for a measure of general ND (FTND).
Conclusions: These findings provide initial evidence that ND phenotypes map on to neural substrates underlying basic cognitive processes. Specifically, the results suggest that the tendency toward inflexibility of smoking behavior is inversely related to brain circuitry activated during the control of prepotent responding, and further suggests such inflexibility is mediated via striatal habit learning areas.
Financial Support: Research funded by a grant from the National Institute on Drug Abuse (1R01-DA025876)

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CHARACTERIZING SMOKING TOPOGRAPHY OF CANNABIS IN HEAVY USERS.

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Aims: Self-reported measures of cannabis use have not been validated against objective measures and little is known about the smoking topography characteristics of cannabis users. The current study was conducted to directly compare subjective and objective measures of cannabis use, as well as to assess whether aspects of cannabis smoking topography (e.g. puff volume) predict withdrawal or craving severity during abstinence.
Methods: Participants (N=20) completed an inpatient study in which they alternated between periods of ad-libitum cannabis use and abstinence. Measures of self-reported cannabis use, smoking topography, craving, withdrawal, and sleep measures were collected.
Results: Consumption of cannabis and characteristics related to cannabis smoking were stable within subjects over five days of ad-lib self-administration. Puff volume and duration decreased with successive puffs on a given cannabis cigarette. Total volume of cannabis inhaled during ad-lib periods was significantly correlated with self-reported cannabis use during the month prior to admission using the Timeline Follow-Back (TLFB) method (r = 0.49). Significant correlations were also observed between topography measures (total volume, average volume, peak flow of inhalation) and self-reported total withdrawal severity, objective measures of sleep disturbance (sleep latency, efficiency) and cannabis craving during abstinence (r = 0.48 - 0.62). Greater amounts of cannabis intake were associated with higher withdrawal severity.
Conclusions: The decreased puff volume and duration observed within a cannabis cigarette are consistent with smoking patterns for tobacco users, and suggest within cigarette dose titration by the user. The positive association between amount of cannabis consumed in the laboratory and self-report of smoking patterns in the natural environment via TLFB supports validity of the self-report measure of cannabis use. Finally, the significant correlations between amount of cannabis smoked and severity of craving and withdrawal supports the expected dose-dependent relationship between these factors.
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ADDRESSING GLOBAL DRUG POLICY.

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Aims: The global spread of drug abuse continues unabated despite ongoing multinational responses and implementation of a broad spectrum of drug policies. Yet science-based policy is seldom applied or promulgated. Instead we see stubborn reliance upon the use of outdated criminal codes.
Methods: Funding remains disproportionately skewed toward supply reduction policies, while demand reduction policies are undervalued and under-funded. It is imperative to redress this imbalance. Vigorous, even hypertrophic, supply-side policy-making cannot compensate for the stunting absence of attention given to science-based, demand-side policy development.
Results: We seek an opportunity to begin anew in addressing these global issues. Through the leadership of NIDA and allied research enterprises, we have created a foundation of robust, evidence-based, demand-side research that provides unequivocal guidance for use by international agencies, federal governments, municipalities, and communities.
Conclusions: Governments are recognizing the usefulness of scientific research as a basis for policy formulation. They are actively soliciting the counsel and expertise of leading drug abuse researchers as they advance new policies and forge new solutions. There is increasing appreciation for the critical volume of scientific evidence that has accrued and for the favorable global dissemination of drug abuse research. Nations are able to apply, validate, expand, and amplify research "lessons learned" from other nations. Exemplary drug abuse programs and policies are likewise available for adoption and adaptation.
This is a welcome development. Drug abuse researchers should embrace these new avenues of opportunity for sharing their knowledge, expertise, dedication, and commitment globally. We have a chance to leverage our research contributions in a manner that has worldwide significance. This is completely appropriate, given the international nature and scope of the drug abuse challenge, and the compelling need for science-based policy.
We will bring our own international experiences from countries such as China, Costa Rica, and Colombia to bear on this discussion.
Financial Support: n/a

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IMPULSIVITY, STRESS AND DEPRESSION AMONG CIGARETTE SMOKERS IN COMMUNITY CORRECTIONS: RELATION TO SUICIDAL BEHAVIOR.

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Aims: Suicide is a leading cause of death among individuals in the criminal justice system, but few studies have investigated the factors associated with suicide, particular among individuals under community corrections supervision.
Methods: 107 participants under community correction supervision and enrolled in a clinical trial for smoking cessation were administered measures to assess the role of impulsivity, depression, and stress on smoking cessation; suicidal behavior history was collected and was examined in the context of these measures.
Results: Participants were 38.6+10.3 years of age, 49.5% male, 40.8% Caucasian with about a high school level education (M=11.9 years; SD=2.2) and a Full Scale IQ estimate of 92.5; SD=12.7). 37.9% reported a history of suicidal behavior (26.3% attempters; 11.6% ideators only). Females were more likely than males to have attempted suicide in the past (37.7% v. 13.0%) and to have a history of ideation alone (13.2% v. 7.4%; p=0.004). Participants without a history of suicidal behavior had the lowest scores on the CES-D (M=12.8; SD=9.8), followed by attempters (M=18.3; SD=10.4) and then ideators (M=21.2; SD=14.1; F=4.6, p=0.012). Similarly, individuals with no suicide history reported the lowest levels of stress (M=56.8; SD=11.0), ideators reported intermediate levels of stress (M=61.8; SD=16.0) and attempters reported the highest levels of stress (M=64.0; SD=9.2; p<0.02). On the BIS subscales of self-control and non-planning impulsiveness, ideators scored the lowest (indicating less impulsiveness; M=13.3 and M=25.8, followed by individuals with no suicide history (M=14.2 and 26.8) and attempters (M=16.4 and 29.2; both p's<0.05).
Conclusions: This study demonstrates the important link between depressive symptoms, stress, and impulsivity to historical suicidal behavior and suggests that these factors remain high, even when patients are not in acute suicidal crisis. Interventions are needed that seek to teach coping skills and reduce depressive symptoms as a way of decreasing overall suicide risk.
Financial Support: Supported by University of Alabama at Birmingham Psychiatry Departmental Funds.

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USING FMRI TO EVALUATE CHANGE LANGUAGE IN EMERGING ADULTS: A TRANSLATIONAL PERSPECTIVE.

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Aims: We evaluated the relative strength of CT and ST with heavy drinking EAs during an fMRI-based cue-exposure, hypothesizing that CT would be associated with reduced activation (relative to ST) in neural reward areas.
Methods: Thirteen heavy drinking EAs (50% male; 46% Caucasian; 32% Hispanic) were enrolled. All received one audio-recorded MI session, followed by an fMRI scan within 1 week. EAs were re-presented with their in-session CT and ST statements visually (in written format) and aurally (replaying their statements) during the fMRI alcohol cue-exposure paradigm.
Results: This sample was heavy drinking, as evidenced by past month of alcohol use (M=6 drinks/drinking day), alcohol-related problems (M RAPI=15.5), and hazardous drinking (M AUDIT=10.3). Significant differences emerged in response to the simulated alcohol (non-alcoholic beer) vs. the appetitive control condition. Participants evidenced significantly greater activation during the ST (z=1.9; max z=4.34; caudate, hippocampus, parietal lobules) compared with the CT condition (z=2.3; 0 areas significantly activated) during the simulated alcohol cue.
Conclusions: These results indicate that CT effectively inhibits activation in salient reward areas in a sample of heavy drinking EAs. These data provide preliminary biological support of the psychosocial findings, underscoring the importance of EA utterances of change talk.
Financial Support: This research was supported by DE-FG02-08ER64581 (PI: Feldstein Ewing).

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PEPTIDE DISRUPTION OF THE SEROTONIN (5-HT) 5-HT2C RECEPTOR INTERACTION WITH PROTEIN PHOSPHATASE AND TENSIN HOMOLOGUE DELETED ON CHROMOSOME 10 (PTEN) IS FUNCTIONALLY IMPORTANT TO THE 5-HT2CR SIGNALOSOME.

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Aims: Central 5-HT2CR plays an important role in psychological disorders marked by impulsive-compulsive traits (e.g., addiction, eating disorders), and strategies to augment 5-HT2CR signaling may prove therapeutically useful in such disorders. The goal of the present study was to detail the structural and functional significance of the protein:protein interaction between 5-HT2CR and PTEN, and to test the hypothesis that a small peptide fragment of the 5-HT2CR (3L4F; Pro283-Arg297) will compete with the PTEN for binding to 5-HT2CR and enhance 5-HT2CR signaling.
Methods: 5-HT2CR function was established in agonist-stimulated mobilization of intracellular calcium (Cai++) in CHO cells stably expressing the 5-HT2CR. We developed a novel split luciferase complementation assay (LCA) to validate that the 5-HT2CR and PTEN proteins are in direct contact in live cells.
Results: The 3L4F peptide enhanced 5-HT-stimulated intracellular Cai++ efflux in a concentration-related manner. The LCA detected a direct interaction between 5-HT2CR:PTEN, and preliminary studies suggest that the 3L4F peptide impairs production of the luminescence signal emitted upon formation of the 5-HT2CR:PTEN complex.
Conclusions: These data suggest that the 5-HT2CR:PTEN complex is essential to the efficiency of 5-HT2CR signaling. Molecules that inhibit the 5-HT2CR:PTEN association will be novel pharmacological tools to enhance 5-HT2CR function and may prove therapeutically promising in eating and addictive disorders in which disrupted 5-HT2CR signaling is implicated.
Financial Support: Klarman Family Foundation, UTMB ITS, DA020087, DA030977

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HIV-1 TAT PROTEIN EXPRESSION IN MOUSE BRAIN IMPAIRS LEARNING AND MEMORY PERFORMANCE BUT POTENTIATES THE BEHAVIORAL PSYCHOSTIMULANT EFFECTS OF COCAINE.

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Aims: The functional consequences of the expression of the HIV-accessory protein Tat on learning and memory performance, and the interaction between abused drugs and expressed HIV-1 Tat on behavior are little known. Accordingly, we hypothesized that HIV-1 Tat expression in brain would impair learning and memory performance while modulating the psychostimulant effects of cocaine.
Methods: Using the GT-tg bigenic mouse model, where brain-selective Tat expression is induced by activation of a doxycycline (Dox) promotor, we tested the effects of Tat on novel-object recognition (NOR) as well as cocaine-induced hyperlocomotion and conditioned place preference (CPP).
Results: Uninduced GT-tg and Dox-treated C57Bl/6J mice spent more time exploring a novel rather than familiar object in the NOR test trial. In contrast, mice expressing Tat did not spend more time exploring the novel object in a manner dependent on the duration and magnitude of exposure to Tat protein, suggesting a Tat-induced deficit in learning and memory performance. However, Tat-induced mice demonstrated a significant increase in the locomotor effects of cocaine (10 mg/kg, s.c.), but not saline, over uninduced littermates. Although mice expressing Tat demonstrated saline-conditioned place preferences similar to uninduced littermates, Tat expression significantly increased cocaine-CPP 3-fold. Consistent with this observation, cocaine place-conditioned mice subsequently expressing Tat protein demonstrated a significant increase in cocaine-CPP after an additional cycle of cocaine place conditioning as compared to the response of uninduced mice, although the progression of extinction in Tat-expressing mice was no different. Of interest, subsequent exposure to Tat protein resulted in the reinstatement of an extinguished cocaine-CPP in previously uninduced mice.
Conclusions: Overall, these data suggest that Tat expression in mouse brain produces learning and memory deficits while potentiating the psychostimulant behavioral effects of cocaine.
Financial Support: (None)

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EFFECTS OF THE CANNABINOID JWH-018, A PRIMARY COMPONENT OF K2/SPICE, IN RHESUS MONKEYS.

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Aims: JWH-018 or naphthalen-1-yl-(1-pentylindol-3-yl) methanone is a chemical component of K2/Spice: a mixture of synthetic cannabinoids and an alternative to marijuana. The effects of JWH-018 were compared to Δ9-tetrahydrocannabinol (Δ9-THC) in drug discrimination assays sensitive to the acute and chronic effects of Δ9-THC in rhesus monkeys.
Methods: Monkeys (n=4) discriminated Δ9-THC (0.1 mg/kg i.v.) from vehicle (McMahon, 2006, J Pharmacol Exp Ther 319:1211-1218). Another group (n=5) received daily Δ9-THC (1 mg/kg/12 h s.c.) treatment and discriminated the cannabinoid antagonist rimonabant (1 mg/kg i.v.), i.e., cannabinoid withdrawal (Stewart and McMahon, 2010, J Pharmacol Exp Ther 334:347-356).
Results: Δ9-THC and JWH-018 dose-dependently increased drug-lever responding in monkeys discriminating Δ9-THC; the ED50 values (95% confidence limits) were 0.044 (0.032-0.061) and 0.013 (0.0096-0.018) mg/kg, respectively. Equieffective doses of Δ9-THC (0.1 mg/kg) and JWH-018 (0.032 mg/kg) lasted 4 and 2 h, respectively. Rimonabant (0.32-3.2 mg/kg) dose-dependently shifted the dose-response curves for Δ9-THC and JWH-018 rightward. Schild analyses yielded slopes that did not deviate from unity; there was no significant difference between the apparent pA2 values (95% confidence limits) of 6.64 (6.53-6.76) and 6.72 (6.54-6.89) for rimonabant in combination with Δ9-THC and JWH-018, respectively. In Δ9-THC treated monkeys discriminating rimonabant, the ED50 value of rimonabant was 0.29 (0.21-0.39) mg/kg. The rimonabant ED50 was increased by 1.3-, 3.8-, and 9.7-fold by Δ9-THC at doses of 0.32, 1, and 3.2 mg/kg, respectively, and 1.7- and 4.4-fold by JWH-018 at doses of 0.32 and 1 mg/kg, respectively.
Conclusions: JWH-018 and Δ9-THC act at the same receptors to produce discriminative stimulus effects and JWH-018 can attenuate Δ9-THC withdrawal. JWH-018, aside from being more potent and shorter-acting than Δ9-THC, has acute effects that appear to be indistinguishable from those of Δ9-THC.
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INTERNET DISCUSSION ENDORSING OR DISCOURAGING ABUSE OF PRESCRIPTION OPIOIDS: THE ENDORSEMENT RATIO.

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Aims: Internet monitoring is generally part of pharmaceutical surveillance programs. The Internet is a "sensitive" data source that may reflect trends and preferences among recreational abusers of pharmaceutical products. Internet discussions reflect unvarnished sentiments (likes and dislikes) of abusers about Rx products. Qualitative observations suggest these sentiments vary consistently by Rx opioid product. This presentation describes efforts to systematically characterize the extent to which specific products are endorsed or discouraged for abuse by Internet communities.
Methods: We developed the "endorsement ratio" (ERo) to capture the sentiment expressed about specific Rx opioid products, allowing for a relative ranking of the endorsement for abuse of products. Posts were drawn from the Web Informed Services (WISTM), a NAVIPPRO data stream, which monitors eight drug abuse online forums. Posts were selected discussing three Rx opioid products thought to be widely discussed and generally desirable for abuse (OxyContin®, Dilaudid®, and Vicodin®) along with posts of two products that are less widely discussed online (Ultram® and Nucynta®). Samples of ≈1,000 posts each for the widely discussed products were randomly selected. All posts relevant to Ultram® and Nucynta® (≈100 each) were identified. Following a codebook, reliable coders categorized posts as encouraging abuse, discouraging, mixed or unclear. The ERo = proportion of messages endorsing the product/proportion of messages discouraging it.
Results: Preliminary analyses suggest that abusers endorsed Dilaudid® (ERo = 1.765, SE = 0.156) the most followed by OxyContin® (ERo = 1.710, SE=0.152) and Vicodin® (ERo = 1.080, SE=0.095). Ultram® (ERo = 1.000, SE=0.246) had an equal ratio of endorsement and discouragement, and Internet posts for Nucynta® (ERo = 0.926, SE=0.257) appeared to discourage its use more than endorse it.
Conclusions: The endorsement ratio is offered as a possible way to reflect the essential sentiment conveyed by the online community of abusers about specific Rx opioid products.
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ARE DENTISTS READY TO OFFER SCREENING, BRIEF INTERVENTION AND REFERRAL TO TREATMENT FOR SUBSTANCE USE?

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Aims: Dentists are a largely untapped resource for identifying and assisting patients with substance use disorders. Substance use has substantial effects on oral health, and for many individuals the dental visit may be their only contact with the health-care system. We surveyed dentists to learn whether they might play a role in substance use screening and interventions.
Methods: All dentists active in the PEARL practice-based research network were invited to complete a web-based survey in summer 2010. The 41-item survey assessed clinic policies and dentists' practices, attitudes, and perception of barriers regarding screening, counseling and referrals for substance use.
Results: 143 dentists completed the survey (68% response rate). They had been in practice for a median of 26 years (IQR=12), and most were generalists (84%) in urban/suburban settings (90%). Almost all respondents felt it was important to screen patients for tobacco (99%), alcohol (92%) and illicit drug (93%) use, though actual screening rates were lower (78%, 65% and 55%, respectively). Counseling or referrals were infrequently provided for alcohol (29%) and drugs (25%), but were more common for tobacco (63%). The most frequently identified barrier to addressing substance use was insufficient knowledge/training. Other barriers were lack of referral sites, staff resistance, and time constraints. If reimbursement were available, many dentists said they would offer counseling and assistance for tobacco (67%), alcohol (52%), and drugs (48%); an affirmative response was significantly more likely among the 43 dentists who saw Medicaid patients (P<0.01).
Conclusions: Dentists recognize the importance of screening for substance use, but lack the clinical training and systems that might allow them to intervene. If these barriers were reduced, dentists could be willing partners in addressing substance use disorders.
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INVESTIGATING THE COMPLEX RELATIONS BETWEEN CULTURE AND SUBSTANCE USE: A PRELIMINARY MODEL WITH HIGH RISK ADOLESCENTS.

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Aims: Many questions exist related to the source and nature of differences in substance use disorders (SUD) across cultures. Several cultural factors have been posited as protective for minority youth, including cultural identification. With a diverse sample of justice-involved youth in the southwest, we posited that greater cultural identification would be associated with lower levels of alcohol and marijuana use for Hispanics, and would be unrelated to level of substance use for Caucasians.
Methods: Eighty one alcohol-using youth (M age=16; 75% male; 62% Hispanic; 20% Caucasian) completed a set of measures on demographics, SUD (Timeline Followback), and cultural identification (primary language preference; Multigroup Ethnic Identity Measure). The proposed model was evaluated using SEM.
Results: This was a high risk sample, as evidenced by their justice involvement (M age of first arrest=13; M number of arrests =3) and SUD history (M age of first alcohol use=12; M age of first marijuana use=11), and past month quantity (M drinks per drinking day=6; M hits per marijuana use days=16) and frequency (M number of drinking days=5; M number of marijuana use days=14). The model, including cultural identification and SUD variables, fit the data adequately (CHI=276.08; TLI=.91; rmsea=.06; CFI=.93). The relation between the cultural factors and SUD was more complex than predicted. Specifically, identification with Caucasian cultures was significantly and positively associated with level of marijuana, but not alcohol use. And, identification with Hispanic cultures was significantly and positively related to alcohol, but not marijuana use.
Conclusions: There are few empirically supported SUD interventions for minority youth. These preliminary data underscore the complexity of different patterns of use across cultures and substances. These data highlight the importance of examining these relations to guide the development of efficacious interventions for cultural minority youth.
Financial Support: R01AA017878-01A2 PI: Feldstein Ewing

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EFFECTS OF BUSPIRONE ON THE REINFORCING EFFECTS OF COCAINE AND COCAINE + NICOTINE POLYDRUG COMBINATIONS IN RHESUS MONKEYS.

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Aims: Stimulant dependence remains one of the most significant drug abuse disorders, and there is no universally accepted medication for managing cocaine abuse. Additionally, because most cocaine users also smoke cigarettes, an ideal pharmacotherapy would target concurrent cocaine and nicotine abuse. Buspirone is a clinically available, non-benzodiazepine anxiolytic medication thought to act through serotoninergic and dopaminergic systems. In clinical laboratory studies, it has been evaluated as an anti-smoking medication, and in preclinical laboratory studies it has been shown to reduce cocaine self-administration following acute treatment in rhesus monkeys. The purpose of the present study was to evaluate the effectiveness of chronic buspirone treatment on self-administration of cocaine and cocaine + nicotine combinations.
Methods: Four adult rhesus monkeys (Macaca mulatta) were trained to self-administer cocaine and food during alternating periods under a second-order schedule of reinforcement seven days per week. Buspirone was administered intravenously through one lumen of a double lumen catheter for 23 hours each day for 7-10 consecutive days. Drug- and food-maintained responding was evaluated during chronic treatment with buspirone. Each 7-10 day test condition was followed by period during which monkeys were returned to baseline conditions for at least 5 days and until behavior became stable.
Results: Buspirone dose-dependently reduced responding maintained by cocaine and cocaine + nicotine combinations, but did not reduce food-maintained responding.
Conclusions: These preliminary findings suggest that buspirone selectively attenuates the reinforcing effects of cocaine and cocaine + nicotine polydrug combinations without reducing food-maintained behavior.
Financial Support: This research was supported by R01-DA026892 and R01-DA024642 (NKM) from the National Institute on Drug Abuse, NIH.

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MDMA-INDUCED INCREASES IN BLOOD PRESSURE ARE NOT MEDIATED BY α-ADRENERGIC MECHANISMS AND ARE NOT DUE TO ELEVATED PERIPHERAL VASCULAR RESISTANCE.

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Aims: MDMA is a sympathomimetic psychostimulant with potent cardiovascular (CV) effects. Because the mechanisms of adrenergic modulation of cardiac physiology are not well characterized we used impedance cardiography (IC), a non-invasive method that measures stroke volume (SV), cardiac output (CO) and systemic vascular resistance (SVR), to assess interactions between MDMA and the α-adrenergic inverse agonist prazosin.
Methods: Eight males and eight females, all healthy and MDMA-experienced, received 1.5 mg/kg oral MDMA alone and in combination with 1-2 mg prazosin in a placebo-controlled, within-subjects randomized controlled trial. IC measures were obtained frequently from 0-8 hours post dose. Change scores were analyzed by ANOVA.
Results: MDMA increased heart rate (HR) by 25 bpm ($p<001$), CO by 1.75 L/min ($p<0.01$) but did not alter SV or SVR. Compared to MDMA alone the combination of MDMA + prazosin further increased HR by 24 bpm ($p<0.001$) and CO by 3.3L/min ($p<0.02$). MDMA increased systolic and diastolic blood pressure (SBP, DBP) by 26 mmHg ($p<0.001$ each); prazosin attenuated MDMA effects on DBP by 9.3 mmHg ($p<001$) but did not alter SBP.
Conclusions: MDMA increases HR, producing elevations in CO. The hypertensive effects of MDMA are not due to elevated peripheral vascular resistance and the blood pressure effects of MDMA are not attenuated by α-adrenergic blockade, suggesting that MDMA may produce CV effects through non-α-adrenergic mechanisms.
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THE ROLES OF NICOTINIC AND MUSCARINIC CHOLINERGIC RECEPTORS IN COST-BENEFIT DECISION MAKING.

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Aims: Psychopathological conditions in which cost-benefit decision making is impaired include schizophrenia, ADHD, and addiction. Although a link between cholinergic neurotransmission and these conditions has been shown, little is know about the role of cholinergic systems in cost-benefit decision making. It was predicted that manipulations of cholinergic neurotransmission would affect cost-benefit decision making.
Methods: Male Long-Evans rats were trained in either a "probability discounting" task (n = 15) or a "delay discounting" task (n=16). The effects of acute administration of cholinergic drugs were evaluated. Another group of rats (n = 16) was trained on both tasks, and relationships between decision making and nicotinic receptor binding levels were evaluated using radioligand binding. Performance on discounting tasks was assessed using repeated measures ANOVA, while Pearson's correlations evaluated relationships between discounting and binding levels.
Results: In the probability discounting task, nicotine increased choice of the large risky reward. In the delay discounting task, the muscarinic receptor antagonist atropine increased preference for the small immediate reward. In the receptor binding study, increased preference for the large reward in both discounting tasks was correlated with decreased α4β2 nicotinic receptor levels in the nucleus accumbens shell. Increased preference for the large reward in the delay discounting task was also significantly correlated with decreased α4β2 nicotinic receptor levels in the dorsal hippocampus and α7 nicotinic receptor levels in basolateral amygdala.
Conclusions: These experiments show that the cholinergic system is involved in cost-benefit decision making and may prove as a useful target for the treatment of psychopathological conditions involving impaired cost-benefit decision-making.
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PSYCHOLOGICAL DISTRESS AND DEPRESSION / ANXIETY DIAGNOSIS AMONG PATIENTS IN SUBSTANCE ABUSE TREATMENT CENTERS IN SEVEN COUNTRIES OF LATIN AMERICA AND ONE IN THE CARIBBEAN: POLICY AND PROGRAM IMPLICATIONS.

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Aims: There is little to no comparative research exploring mental disease comorbidity and drug abuse in Latin America & the Caribbean. We conducted a multicenter study on the frequency of psychological distress among patients in treatment for illicit drugs and alcohol abuse in eight countries. We describe the current diagnosis of anxiety and depression.
Methods: We recruited 1,073 adult patients at specialized centers, where they filled out a questionnaire or were interviewed. We evaluated psychological distress through the Kessler's K-10 scale.
Results: Male individuals predominated in all sites. Age varied from 18 to 86 years old. Current diagnosis of anxiety ranged from 6.0% to ~60.0%, being reported by 30.0% to 40.0% of the patients in most sites. Current diagnosis of depression varied from 6.6% to 42.4%; range in most of places: 20.0% - 35.0%. High and very high levels of psychological stress scale were: Montevideo-Uruguay: 75.8%; N=128; followed by León-Nicaragua: 75.2%; N=36; Guatemala: 71.5%; N=81; Brasilia-Brazil: 70.1%; N=164; Macaé-Rio de Janeiro-Brazil: 61.0%; N=58; Chile: 48.6%, N=107; Panamá: 37.8%, N=167; Managua-Nicaragua: 33.9%, N=130; Paraguay: 26.7%; N=149.
Conclusions: As psychological distress prevalence suggests higher rates of comorbidity in most study sites, less than half of the patients have been diagnosed for depression and anxiety. Our data provide evidence to address comorbidity therapy at health care services.
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AN INTERNET-BASED GROUP CONTINGENCY MANAGEMENT PROGRAM TO PROMOTE SMOKING CESSATION.

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Aims: Aim 1: Evaluate the feasibility and acceptability of combining Internet-based contingency management with monetary group contingencies and online peer support.
Aim 2: Test the hypothesis that group contingency management will promote higher rates of smoking cessation relative to rates observed during a baseline control condition.
Methods: Thirteen participants were divided into 5 groups or "teams" (n = 2-3 per team). Each participant submitted video recordings of breath CO measurement twice daily via the Internet. Participants could monitor their teammates' progress and communicate with one another through a user-friendly website. During a 4-day tapering condition, vouchers exchangeable for merchandise and gift cards were delivered contingent on gradual reductions in breath CO. During a 10-day abstinence induction condition, vouchers were contingent on abstinence (CO ≤ 4 ppm). In both treatment conditions, voucher delivery was contingent on individual and team performance. A nonconcurrent multiple baseline design was employed to evaluate treatment effects.
Results: Less than 1% of CO samples submitted during baseline were ≤ 4 ppm, compared to 57% submitted during abstinence induction. Most participants regularly communicated with one another on the online peer support forum (128 posts; *M* number of posts per participant = 9.8, *SD* = 5.7). Sixty-five percent of the posts were rated as positive by independent observers. Participants rated the intervention favorably on a treatment acceptability questionnaire.
Conclusions: Internet-based group CM is a feasible, acceptable, and efficacious method to promote abstinence from cigarette smoking.
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SUPPORTING RECOVERY IN THE COMMUNITY: PRELIMINARY OUTCOMES OF CLIENTS PARTICIPATING IN THE PHOENIX HOUSE BRONX COMMUNITY RECOVERY CENTER.

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Aims: The Phoenix House Bronx Community Recovery Center (BCRC) was developed to promote recovery capital and sustained abstinence from alcohol and drug use by offering an array of peer- and professionally-delivered recovery support services and establishing collaborations with agencies that provide other community-based services to clients living in the Bronx. This presentation highlights preliminary findings from 99 clients who completed intake and 6-month follow-up GPRA interviews between March 2009 and November 2010 (77% of those who were due for follow-ups).
Methods: Multilevel logistic regression analysis was used to examine differences in various domains of functioning (substance use, general health, mental health, employment/education, legal status, and social connectedness) between intake and 6-months follow-up interviews.
Results: Clients showed improvements in a variety of domains. At follow-up, clients were less likely to report using illegal drugs (OR=0.2, p=0.005) and committing crimes in the past 30 days (OR=0.3, p=0.008). Clients were more likely to report being employed (OR=3.6, p=0.024) and attending faith-based, self-help groups for recovery (OR=2.8, p=0.014).
Conclusions: Clients participating in the BCRC made significant gains in decreasing drug use and criminal activity between intake and 6 month follow-up interviews. They were also more likely to be employed and attending faith-based, self-help groups. It should be noted that clients participating in recovery centers have generally made a commitment to recovery and have usually received treatment prior to engaging in recovery support services. Still, these findings provide preliminary support for the usefulness of community-based recovery centers to promote recovery capital and reduce substance use.
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PRESCRIPTION DRUG DIVERSION BY PHARMACISTS: MECHANISMS AND AREAS FOR PREVENTION.

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Aims: To highlight mechanisms of prescription drug diversion by pharmacists and determine potential areas to target for prevention efforts.
Methods: A sample of 32 pharmacists (71.9% male) under contract with a state monitoring program for substance-related impairment (22.2% of total being monitored) were invited to participate in guided group discussions. Experienced researchers led the anonymous discussions, which were digitally recorded and transcribed for qualitative analysis using the Grounded Theory method.
Results: In total, 87.5% of the pharmacists admitted misuse of prescription drugs, acknowledging that they diverted from their workplace. Five primary diversion themes emerged: 1) taking expired drugs that could no longer be sold by the pharmacy and were awaiting disposal; 2) using "sleight of hand" techniques to acquire drugs while filling prescriptions or shelving product; 3) assuming responsibility for managing the pharmacy inventory and/or changing inventory records to prevent detection of missing drugs; 4) forging prescriptions for themselves, family members, friends, or customers in order to gain access to the drugs; and 5) as their addiction worsened, blatantly stealing drugs from the pharmacy, even in front of coworkers or video cameras. Although the pharmacists indicated that recently-implemented anti-diversion programs in many workplaces are helpful in curbing these problems, they noted that more effort is needed in most settings, where inventory standards are lax, schedule III-V drugs are not well-monitored, and forged prescriptions (whether written or phone orders) are virtually never questioned or discovered.
Conclusions: Prescription drug diversion is a significant problem for a minority of pharmacists, which negatively impacts public health and safety. Recent efforts to address this problem should be expanded to safeguard pharmacies and the patients they serve.
Financial Support: Research supported by NIDA R01-DA20791 (PI: Cottler), T32-DA-07313-10 (PI: Cottler), and Professionals Resource Network, Inc., an integral arm of the Florida Medical Association.

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THE EFFECT OF PRENATAL COCAINE EXPOSURE AND SEX/GENDER ON ANTHROPOMETRIC GROWTH THROUGH AGES 16-17 YEARS.

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Aims: We investigated the effects of prenatal cocaine exposure (PCE) on offspring anthropometric measurements through 16-17 years of age.
Methods: We longitudinally compared anthropometric measures (height, weight, body mass index [BMI]) from birth through ages 16-17 years among PCE/non-prenatally exposed (NCE) African American children/adolescents who had been born at term (≥37 weeks gestation). Linear mixed model regression analysis compared PCE/NCE growth by gender in height (inches), weight (pounds), and BMI from birth to age 17. Heights and weights were converted to BMI %iles for age and sex for cross sectional analysis at ages 16-17 only.
Results: A total of 9,500 growth data points from the Miami Prenatal Cocaine Study cohort (N = 476, 53% PCE, 48% female) were analyzed. Longitudinal analysis showed PCE females were lighter and shorter at birth versus boys(P =0.01 for both comparisons). This trend continued up to age 14, but then PCE girls were significantly heavier than boys by age 16-17(P =0.05). PCE females had the steepest inclines in BMI growth trajectories from ages 12-14 to 16-17 compared to all groups. Cross-sectional BMI analysis at ages 16-17 showed (1)overall, girls were significantly more likely than boys to be overweight (BMI >/= 85th %ile for age, sex)(45% versus 35%, P =0.04);(2)overall, 21% of both NCE/PCE were obese(BMI >/= 95th %ile for age, sex);(3)26% of both NCE males/females, 25% of PCE females and 16% of PCE males were obese; and (4)obesity almost doubled for both NCE/PCE from 11% at ages 12-14 to 21% at ages 16-17.
Conclusions: Although the influences that impair fetal development and program adult chronic disease remain to be defined, our findings here suggest that PCE girls in particular may be at risk for future onset of cardiometabolic disease due a combination of being born small and later rapid increase in obesity during the teenage years.
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ENHANCING SUBSTANCE ABUSE TREATMENT FOR WOMEN IN DRUG COURT.

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Aims: To test the efficacy of a women's integrated treatment (WIT) curriculum to promote positive behaviors among women offenders (i.e., increased psychological well-being, treatment participation, and reductions in drug use, and recidivism) compared to the impact of the mixed-gender (MG) program.
Methods: 150 women were recruited from four drug court programs. Those who agreed to participate were randomly assigned to one of the two study conditions (WIT or MG treatment programs). The WIT treatment program was gender specific using Helping Women Recover and Beyond Trauma curricula. ANOVA was used to compare the WIT program and the MG program for outcomes represented by a single continuous variable. For categorical and binary outcome variables, chi-square analysis was used. A General Linear Modeling for repeated measures approach was used to consider change over time.
Results: During the first 6 months of treatment, drug court participants received sanctions at equal rates; however, during the second phase of treatment the WIT group received significantly less disciplinary sanctions (WIT mean = .65, s.d.=1.2; MG mean = 1.2, s.d.=1.8, p<.03) compared with those in the MG group. The number of times a sanction resulted in detention in jail was also significantly different between the two groups with WIT participants less likely to be remanded to jail (WIT mean = 1.9, s.d. = 1.2 and MG mean = 2.4, s.d. = 1.5, p < .05). At follow-up, 13% met the criteria for current PTSD (36% at baseline reduced to 9% of the WIT group; 26% at baseline reduced to 18% of the MG group). Moreover, theWIT group reported reduced symptoms for each symptom measured. In contrast, the women in the MG groups reported an increase in re-experiencing of their traumatic event from baseline to follow up, and no change in their other symptoms.
Conclusions: Future studies should continue to assess the provision of specific gender-responsive curricula to determine if the current study findings are replicated.
Financial Support: Supported by NIDA Grant No. DA022149-01.

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COMPARISON OF MATERNAL AND NEONATAL OUTCOME PARAMETERS IN PREGNANT OPIOID-MAINTAINED WOMEN IN A RCT VS. IN STANDARDIZED ROUTINE CARE.

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Aims: The aim of this study was to compare maternal and neonatal outcome of opioid-dependent women maintained on buprenorphine or methadone throughout pregnancy in a RCT (MOTHER-study) with a control group undergoing routine care (standard protocol=SP).
Methods: One hundred and twenty four subjects were included in the comparison analysis of two prospectively followed patient cohorts at the addiction clinic of the Medical University of Vienna, Austria, with n=83 in SP (methadone group n=55, buprenorphine group n=28), and n=41 in a double-blind, double-dummy clinical trial (methadone group n=21, buprenorphine group n=20).
Maternal measurements: supervised urine toxicologies (combined with contingency management in RCT), standardized questionnaires, date/mode of delivery. Neonates: demographical birth data, standardized assessment (modified Finnegan score) of neonatal abstinence syndrome (NAS), required morphine dose, length of stay (LOS).
Results: No significant differences for concomitant consumption occurred in third trimester of pregnancy between the two groups not differing in mean opioid dose at delivery. Neonates in SP needed a significantly higher total morphine dose (p=0.008), had a longer duration of treatment (p=0.051) and LOS (p<0.001). Infants did not differ in birth weight, body length, head circumference or APGAR scores 1'/5'/10'. Infants exposed to buprenorphine showed improved outcome regarding body weight and all NAS parameters compared to the methadone group.
Conclusions: This analysis supports the efficacy of multidisciplinary care in yielding beneficial outcomes for mothers and infants. Higher structured neonatal care in RCTs refers to the requirement of ameliorating standard care. The results confirm the favorable neonatal outcome after intrauterine buprenorphine exposure.
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DEPRESSION AND ABSTINENCE IN EFFECTIVELY TREATED COCAINE DEPENDENCE WITH OTHER MENTAL DISORDERS.

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Aims: Despite high prevalence of co-occurring disorders (CODs) in substance abusers, few studies examine their effects on treatment outcomes for homeless persons. Fewer used effective intervention, reliable/valid measures for CODs, and abstinence. The aim was to examine change in depression, using Structure Clinical Interview for DSM-IV (SCID) and Beck Depression Inventory (BDI) at admission. Examined was response to effective substance abuse treatment in a randomized treatment trial, and how depression relates to a rigorous abstinence outcome at 6 months.
Methods: Methods Participants completed BDI and SCID at admission (n=203).Two independent variables were defined, related to depression and abstinence response to effective treatment, ignoring original treatment assignment. Consecutive weeks abstinent over 6 months (CWA) was measured by 3 weekly (MWF) urine toxicology tests for cocaine, marijuana, and alcohol. The effects of depression (baseline BDI≥12) on CWA, and of abstinence (CWA≥12 wks) on 6-month BDI scores were assessed by ANOVA. The last observation carried forward was used for missing BDIs at 6 mos. Missing abstinence data allowed excused missing without interference with a CWA string. Unexcused missing tests were treated as non-abstinent. Participants were 72.4 % male. For both genders mean age was 40 (SD 7), mean education was 12 years (SD=1.8). Most common CODs were depressive disorders (42.4%).
Results: Results CWA did not differ significantly (13.9 vs 11.5 weeks [F (1, 201) =2.67, p= 0.10]), for those depressed or not at baseline, but 6-month BDI did differ significantly among those abstinent versus not (14.1 vs 8.0 consecutive weeks, [F (1, 201) =20.1, p< 0.001]).
Conclusions: Conclusions Depression, though not related to reduced abstinence, still responds to effective substance abuse treatment, even where depression is not specifically treated. More depression monitoring during treatment may facilitate more depression treatment goals, and lead to better outcomes.
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ACCUMBENS HISTONE DEACETYLASES ACTIVELY REGULATE COCAINE-SEEKING IN COCAINE-EXPERIENCED MICE.

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Aims: Repeated cocaine experience produces an enduring decrease in histone acetylation within the mesocorticolimbic circuit that can facilitate the development of cocaine addiction-related behaviors in animal models. However, the role for NAC histone acetylation in the maintenance or expression of cocaine-seeking behavior following a history of cocaine experience is under-characterized.
Methods: The present study employed viral gene delivery and pharmacological approaches, respectively, to determine the effects of increasing the activity of the class II histone deacetylase HDAC5 and decreasing the activity of class I histone deacetylases (HDACs) within the NAC upon the expression of a cocaine-conditioned place-preference (CPP) in mice elicited by the repeated pairing of 15 mg/kg cocaine.
Results: NAC HDAC5 over-expression during short-term (3-day) withdrawal from repeated cocaine reduced the magnitude of cocaine CPP to 1/3rd that expressed by control animals. Conversely, intra-NAC infusion of 100 microM of the class I HDAC inhibitor N-(2-aminophenyl)-4-[N-(pyridine-3-ylmethoxy-carbonyl)aminomethyl]benzamide (MS275) doubled the magnitude of cocaine CPP expressed at 3 days withdrawal. Neither NAC manipulation influenced locomotor activity during CPP testing.
Conclusions: These findings confirm an active role for NAC HDAC5 in regulating cocaine-seeking behavior in cocaine-experienced animals and further the notion that a cocaine-induced decrease in histone acetylation within the NAC is an important epigenetic mechanism contributing to the persistence of addiction.
Financial Support: NIDA grants DA024038 to KKS and P01 DA08227 and R01 DA07359 to EJN.

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ADVANCING THE RHESUS MONKEY MODEL FOR OPIOID RESEARCH: DISCOVERY OF A NOVEL NONSYNONOMOUS VARIANT IN THE KAPPA OPIOID RECEPTOR GENE.

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Aims: Rhesus monkeys are a widely used model in addiction research because of their behavioral, physiological and genetic similarities to humans. We have found that rhesus monkeys harbor polymorphic variation in genes implicated in addiction that affect gene expression or protein structure comparably to variants in humans. The mu-opioid receptor gene (OPRM1), for example, harbors a single nucleotide polymorphism (SNP), A118G (N40D), which in humans alters receptor structure, ligand affinity and therapeutic response to naltrexone, whereas the rhesus monkey OPRM1 harbors a C77G (P26R) SNP that, although altering a different amino acid in the N-terminal arm of the protein, nevertheless has similar effects on protein function. We have shown in alcohol drinking rhesus monkeys that animals with the 77G allele not only drink more alcohol but also have a better response to naltrexone, as in human alcoholics (Vallender et al., DAD 109:252, 2010). Here, our aim was to screen the rhesus monkey kappa opioid receptor gene (KOR) for polymorphic variation.
Methods: Sequencing of KOR exons was performed on 48 unrelated Indian rhesus DNA samples. An additional 220 DNA samples were genotyped using a FRET-based allelic discrimination assay.
Results: We discovered novel SNPs in the rhesus monkey kappa opioid receptor: A627G and G902A. While the former is silent, the latter is nonsynonomous (S301N) and the minor allele creates an additional glycosylation site in the third extracellular loop of the receptor. The G902A SNP has a 21% minor allele frequency in Indian rhesus (n=228) and a 1% minor allele frequency in Chinese rhesus (n=40). Pharmacological characterization of each allele stably expressed in HEK293 cells, as well as genotype/phenotype assessments, are currently being pursued.
Conclusions: As our functional understanding of rhesus monkey KOR and OPRM1 SNPs increases so too does our ability to model the diseases of addiction, predict drug responses and develop pharmacogenomic therapeutic treatments.
Financial Support: AA019688 (EJV); MH077995 (GMM); DA025697 (GMM); RR00168 (NEPRC)

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ENHANCEMENT OF MORPHINE'S EFFECTS ON PAIN-SUPPRESSED WHEEL-RUNNING BY A FAAH INHIBITOR.

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Aims: Both fatty acid amide hydrolase (FAAH) inhibitors and anandamide (AEA) uptake inhibitors limit the degradation of endogenous cannabinoids, and produce type 1 cannabinoid receptor (CB1) mediated antinociception. There is evidence that endogenous signaling via CB1 modulates the antinociceptive effects of opioids. This study examined the effects of a FAAH inhibitor, URB597 and an AEA uptake inhibitor, AM404 on morphine in a model of pain-suppressed wheel-running in mice.
Methods: C57BL/6 mice were individually housed in polycarbonate cages equipped with running wheels. Testing occurred after two weeks of acquisition and stabilization of wheel-running. During control sessions, mice were injected with saline and wheel-running (revolutions) was recorded for 30 m. During test sessions, mice were injected with 0.56% acetic acid prior to recording wheel-running. During these sessions, morphine (0.32 – 3.2 mg/kg), the CB1 agonist, CP55940 (0.01-0.1), URB597 (0.32-10.0), AM404 (1.0-10.0) or vehicle were administered prior to acetic acid. In experiments examining the cannabinoid compounds in combination with morphine, fixed-doses of CP55940, URB597 and AM404 were administered prior to a range of doses of morphine.
Results: Intraperitoneal injection of acetic acid completely suppressed wheel-running. URB597, AM404, and morphine attenuated the suppression of wheel-running by acetic acid injection, whereas the CB1 agonist CP55940 did not alter pain-suppressed wheel-running. URB597 produced an upward shift in the morphine dose-effect curve, but neither AM404 nor CP55940 altered morphine's effects on pain-suppressed wheel-running.
Conclusions: These data provide further evidence that drugs which alter endogenous cannabinoid signaling have antinociceptive effects and are consistent with findings suggesting that morphine's effects are modulated by endogenous cannabinoid signaling at the CB1 receptor. The effects of the CB1 agonist, CP55940, in this model are consistent with the its disruptive effects on locomotor activity.
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PPARγ AS A THERAPEUTIC TARGET IN DRUG ABUSE.

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Aims: In this study we will delineate the time course of PPARγ and ERK alterations during the establishment of cocaine self administration, its extinction, and its reinstatement followed by testing the hypothesis that PPARγ agonism during the self administration paradigm will decrease cocaine self administration upon representation of the cocaine self-administration cues.
Methods: Studies will use an FDA-approved PPARγ agonist to determine if stimulating this newly-identified CNS signal transduction molecule will decrease cue-induced reinstatement of cocaine self-administration as a model of cocaine abstinence. We will also determine if PPARγ agonism effectively blocks increased locomotor activity in a cocaine behavioral sensitization paradigm.
Results: Here we present new data validating the biological relevance of the target PPARγ which is elevated in male Sprague Dawley rats after cocaine self-administration. We evaluated the expression of PPARγ and ERK in the brains of rats withdrawn from repeated cocaine self-administration or vehicle (sham) groups. We were interested in learning if PPARγ or pERK were reduced in nuclear extracts of rats experiencing 30 days forced abstinence in comparison to 1 day forced abstinence and cue reinstatement. This would indicate that PPARγ agonism with RTZ may influence subsequent self administration behavior following prolonged forced abstinence. We noticed a significantly lower amount of nuclear PPARγ in both prefrontal cortex (PFC) and hippocampus (HIP) samples following 30 days forced abstinence/cue reinstatement compared to day 1 forced abstinence/cue reinstatement.
Conclusions: This translational model couples preclinical evaluations of behavior and neural signaling in an established animal model for cocaine self-administration. Our overall goal is to identify a potential therapeutic for stimulant addiction.
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EFFECTS OF CHRONIC NICOTINE USE ON COCAINE USE.

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Aims: The purpose of this study was to examine the effects of chronic cigarette smoking on treatment outcome in a cocaine dependent population.
Methods: Our sample consisted of 44 individuals (84% male, 41% African American, 34% Caucasian, 23% Hispanic and 2% Asian; age = 43 ± 9) who completed a 14-week double-blind, placebo-controlled outpatient treatment trial examining the effects of Adderall-XR and Topirmate on cocaine dependence. All participants met DSM-IV-TR criteria for cocaine dependence as assessed by the SCID. Groups were defined by cigarette smoking status: chronic smokers (CS) reported daily use on all 28 days prior to baseline (n = 24) and nonsmokers (NS) indicated no use in the 28 days prior to baseline (n = 20). Both groups were similar in demographics and baseline cocaine use patterns. Self reported cocaine use was collected using a timeline follow-back. The primary outcome measure was >50% reduction in cocaine use during the last 28 days of the study compared to the 28 days prior to study entry.
Results: Binary logistic regression revealed no significant differences between the smoking groups on treatment outcome, however, among the CS group there was a trend with those who achieved >50% reduction in cocaine use increasing the number of cigarettes smoked at the end of the study (p = .074). There was no significant effect of treatment arm (p=.214) between the two groups. Analysis of secondary outcomes showed no significant differences between CS and NS in their reduction of cocaine use as defined by number of days of use and dollars used per day.
Conclusions: Although not significant, these results support previous findings that there is a trend among individuals who decrease cocaine use to substitute or compensate by increasing nicotine use.
Financial Support: This research was supported by NIDA grant RO1DA022217

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EXECUTIVE FUNCTION AT 12 YEARS IN PRENATALLY COCAINE-EXPOSED CHILDREN.

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Aims: To assess differences in caregiver reported executive function in prenatally cocaine exposed (PCE) and non cocaine-exposed (NCE) 12 year old children.
Methods: One Hundred and sixty-four (164 PCE) and 169 (NCE) primarily African American, low SES children participated in a longitudinal study investigating effects of PCE. Executive function (EF) was assessed using the Behavior Rating of Inventory of Executive Function (BRIEF), caregiver report. T-scores of the Behavioral Regulation Index (BRI)(inhibit, shift and emotional control) and Metacognition Index (MI)(initiate, working memory, planning, organization of material and self monitoring) were analyzed. T tests and Multiple regression analyses were used to assess the effects of PCE on EF, controlling for covariates.
Results: Higher mean BRI (51.6 + 10.8 vs 55.1 + 11.1) and MI (52.6 +12.5 vs 56.1 + 12.6) scores were reported for children with PCE. Problems of metacognition were associated with higher amounts of PCE ($p<.007$) after control for covariates. Among the MI subscales PCE predicted poorer initiative ($p<.008$) and self monitoring ($p<.006$). There was a significant cocaine by gender interaction for initiative ($p<.004$) with PCE females having less initiative. Greater PCE was related to poorer organization of materials ($p < .001$). There were no significant prenatal cocaine effects on the BRI or its subscales.
Higher levels of prenatal alcohol exposure were related to inability to inhibit behavior ($p<.03$). Greater caregiver reported psychological distress was associated with higher ratings on all BRIEF broadband and subscales ($p<.001$).
Conclusions: Caregiver report of executive function problems indicated that prenatally cocaine-exposed children had more problems initiating activities, self-monitoring and organizing materials. These data suggest that targeted interventions for improvements in metacognitive skills be recommended for high risk children.
Financial Support: NIDA R01-07957

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ADOLESCENT RISK-TAKING AND COCAINE SELF-ADMINISTRATION.

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Aims: Drug use among adolescents is a pervasive problem and adolescence is characterized by excessive risk-taking. Drug use and excessive risk-taking are commonly found to be comorbid; however, it is difficult to disentangle the cause and effect relationships among these variables in humans. Our lab has recently developed a behavioral task in rats to assess risk-taking behavior (the Risky Decision-making Task). We are currently using this task to determine the extent to which adolescent risk-taking predicts drug self-administration.
Methods: Adolescent male Long-Evans rats (P21) 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 which resulted in a small, "safe" food reward and the other which resulted in a large, "risky" food reward that was accompanied by the risk 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%). Upon completion of the Risky Decision-Making Task (P57), rats were allowed to mature and then implanted with an intravenous catheter. Following recovery, animals were allowed to self-administer cocaine HCl for 2 hrs/day.
Results: We have previously reported substantial individual variability in the Risky Decision-making Task, such that performance in adult rats can be reliably characterized as "risk taking" or "risk averse". Similar variability was observed in adolescent rats, suggesting that the task is adaptable for this younger age group. Importantly, preliminary data indicate that during the first four days of cocaine self-administration, there was a significant relationship between performance in the Risky Decision-making Task and cocaine intake, such that rats that chose the large, risky reward more often in adolescence ("risk takers") acquired cocaine self-administration more rapidly.
Conclusions: These data suggest that adolescent risk-taking may be predictive of acquisition of drug self-administration. This predictive relationship suggests a common neural mechanism and may suggest a potential target for prevention treatments.
Financial Support: DA024671 (BS)

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CHARACTERISTICS OF NEWLY ADMITTED METHADONE VS. BUPRENORPHINE PATIENTS.

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Aims: To compare characteristics of patients entering methadone v. buprenorphine treatment programs to determine whether they are attracting different patient populations.
Methods: Participants consisted of two groups of adult heroin-dependent individuals in the Baltimore, Maryland metropolitan area. The first group was entering buprenorphine treatment at either a community health center (CHC) or a mental health center (MHC) and the second group was entering one of two free-standing methadone treatment programs (MTPs). All participants were interviewed at treatment entry using the Addiction Severity Index (ASI) and the Friends Supplemental Questionnaire. Group differences were examined with chi-2 goodness of fit and independent samples t-tests.
Results: The buprenorphine v. the methadone sample (ns = 211 and 231, respectively): had more African Americans ($p < .001$); was older ($p < .001$); had fewer injectors ($p < .001$); and more prior buprenorphine treatments ($p < .001$). Their ASI composite scores were higher for alcohol, medical and psychiatric but not drug problems (all ps < .001). The buprenorphine sample also reported fewer days of heroin use in the past 30 days ($p < .001$); older age of first heroin use ($p=.006$); and more years of heroin and cocaine use (both ps < .03).
Conclusions: There were significant baseline differences between samples. The location of the buprenorphine programs within a CHC and MHC may account for their significantly higher rates of medical and psychiatric problems. The samples' differences in drug use and treatment histories indicate that different community-based treatment options can attract a broader range of people into treatment.
Financial Support: NIDA 1RC1 DA 028407 and NIDA DA R01 013636

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CAN WE PREDICT A PATIENT'S SUCCESS WITH RAPID NALTREXONE INDUCTION?

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Aims: Extended-release (ER) naltrexone has proved promising in the treatment of opioid dependence. Induction onto naltrexone often requires inpatient detoxification, which is a difficult process for many patients to endure, resulting in high dropout rates and relapse. Identifying predictors of successful rapid naltrexone induction can help guide clinicians in the selection of patients likely to succeed. The aim of this study is to compare pre-treatment demographic, clinical, and psychosocial factors between completers and non-completers of a rapid naltrexone induction procedure.
Methods: We conducted a chart review of 76 consecutive research participants, 41 completers and 35 non-completers, admitted to an inpatient unit, for detoxification and induction onto ER or oral naltrexone. We used independent t-tests for continuous variables and Chi square test for categorical variables. All tests were two-tailed and set at $\alpha=0.05$ for this exploratory analysis.
Results: Participants were on average 39 years old, 82% male, predominantly white (53%) or Hispanic (29%) with an average 13 yrs of opioid dependence, and of whom 39% were IV heroin users. Unexpected findings from these data were that completers are more likely to be smokers ($p=0.01$) and without a significant other ($p=0.02$). Several factors such as comorbid psychiatric illness, past abstinence and treatment history, administration route and daily amount used trend towards predictability. Due to a small sample size, however, these factors were not statistically significant.
Conclusions: Conceptualizing the factors that contribute to successful completion of this detox protocol may prove valuable in determining suitability of opioid dependent patients for treatment with ER naltrexone. Further research is needed to elucidate which factors are most predictive of patient success with induction onto opioid antagonist maintenance.
Financial Support: NIDA grant R01-15822-1

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GENDER DIFFERENCES IN PHARMACOKINETICS OF BUPRENORPHINE: INVOLVEMENT OF WEIGHT AND METABOLISM.

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Aims: Gender differences are known to occur in the pharmacokinetics of many drugs. Mechanisms may include differences in body composition, body weight, hormonal status, use of different co-medications, etc. Recently subtle gender-dependent differences in cytochrome P450 (CYP) 3A-dependent metabolism have been demonstrated. Buprenorphine N-dealkylation to norbuprenorphine is primarily performed by CYP3A. We therefore asked the question whether gender-dependent differences occur in the pharmacokinetics of buprenorphine.
Methods: A retrospective examination was made of control (buprenorphine-only) sessions from a number of drug interaction studies between buprenorphine and antiretrovirals. Twenty males and eleven females were identified who had a cocaine negative urine test prior to participation in the control session and were all on the same maintenance dose (16/4 mg) of sublingual buprenorphine/naloxone. An additional five males and two females were on different doses. Pharmacokinetic data from their initial control session were sorted by gender and compared using the two-sample t-test.
Results: Females had significantly higher AUC and Cmax for buprenorphine, norbuprenorphine and norbuprenorphine-3-glucuronide. AUCs were then adjusted for dose per body weight. AUCs relative to dose per body weight, however, were only significantly higher for norbuprenorphine. This also held true when the comparison was expanded to include individuals at all doses.
Conclusions: Gender-related differences exist in the pharmacokinetics of buprenorphine. Both the CYP3A-dependent metabolism and differences in body composition (as measured by weight in this study) contribute to these differences.
Financial Support: This study was funded in part by grants R01 DA10100 (DEM), R01 DA13004 (EMK) and K24 DA023359 (EMK) from the National Institute on Drug Abuse.

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VARIATIONS IN OUTCOMES AND PATIENT CHARACTERISTICS ASSOCIATED WITH METHADONE AND BUPRENORPHINE DOSE.

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Aims: The aims of the current study are to examine associations between: (1) baseline participant characteristics and MMT/BUP dose at treatment-end and (2) MMT/BUP dose and substance use outcomes using data collected in a recently completed study conducted through NIDA's Clinical Trials Network.
Methods: Participants were randomized to receive either BUP (N=740) or MMT (N=529) for 24 weeks at variable clinician-selected doses. Evaluable participants (N=731) included those who were retained in medication treatment for 24 weeks and provided at least 4 liver function tests. For this subset, demographic characteristics were assessed at baseline. Self-reported opioid and cocaine use in the past 30 days and withdrawal symptoms were assessed at baseline and week 24. Urine drug screens were evaluated at week 24.
Results: The evaluable subset of participants included 71.3% of individuals randomized to receive MMT (N=391) and 45.3% randomized to receive BUP (N=340). Clinician-selected dose was stabilized by week 24 with a mean daily MMT dose of 82.9 mg (SD=32.0) and mean BUP dose of 21.3 mg (SD=6.8). MMT dose at week 24 was significantly associated with increased age ($p<0.0001$), Caucasian race ($p=0.002$), and severity of baseline withdrawal symptoms ($p=0.012$). Neither MMT nor BUP dose was associated with baseline drug use. MMT, but not BUP dose was associated with opioid positive urine results at week 24 ($p=0.012$). There were no associations between MMT or BUP dose and self-reported drug use in the 30 days prior to treatment-end.
Conclusions: The current study identified patient characteristics and substance use outcomes associated with clinician-selected dose of MMT in subjects who completed 24 weeks of medication treatment. Lower MMT dose at treatment-end was associated with a greater likelihood of illicit opioid use. Findings suggest that withdrawal severity at baseline may predict need for higher doses of MMT. Further investigation is warranted to elucidate patient characteristics and treatment outcomes associated with MMT and BUP dosing.
Financial Support: This study was sponsored by NIDA grant U10DA013045-10.

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ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SUBTYPES IN COCAINE-DEPENDENT INDIVIDUALS: FREQUENCY AND CHARACTERISTICS.

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Aims: Rates of Attention-Deficit/Hyperactivity Disorder (ADHD) are elevated in cocaine users. However, little is known about the frequency and characteristics of ADHD subtypes in cocaine users, including the stability subtype status from childhood to adulthood.The goal of this presentation is to better characterize ADHD subtypes in cocaine users.
Methods: Participants (N=109) underwent the Conners' Adult ADHD Diagnostic Interview for DSM-IV Part II: Diagnostic Criteria (CAADID-II) as part of an intake evaluation for a placebo-controlled trial of mixed-amphetamine salts in cocaine-dependent individuals. Three ADHD subtypes were: (1) predominantly inattentive (IT); (2) predominantly hyperactive/impulsive (H/IT); (3) combined type (CT); and (4) no diagnosis (ND).
Results: In adulthood, the frequency of ADHD subtypes was: 19.3% (n=21), IT; 13.7% (n =15), H/IT, 42.2% (n=46), CT; and 24.8% (n=27), ND. In childhood, the frequency of ADHD subtypes was: 23.9% (n=26), IT; 8.3% (n=9), H/IT, 36.7% (n=40), CT; and 31.1%, (n=34) ND. Comparison of childhood and adulthood diagnoses revealed substantial change, Bowker's test of internal symmetry (6) = 23.3, p = 0.0007. Contrary to expectation, more subjects fell in the H/IT subtype in adulthood than childhood. In adulthood, the mean (standard deviation) number of symptoms endorsed by subtype was: 11.1 (1.8), IT; 10.3 (2.1), H/IT; 15.5 (1.7), CT; and 4.3 (3.4), ND. Similar symptom rates were seen in childhood. A profile analysis revealed increased endorsement of impulsive symptoms in adulthood.
Conclusions: The distribution of ADHD subtypes in cocaine-dependent individuals was not predominated by any subtype. The prognostic significance of ADHD subtypes in treatment response remains to be determined.
Financial Support: This research was supported by the NIDA grants R01-DA-023651. Dr. Mooney is supported by a NIDA Career Development award K01-DA-019446.

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PROVIDER ACCEPTABILITY OF AUTOMATED ANCILLARY SERVICES FOR BUPRENORPHINE TREATMENT.

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Aims: Automated ancillary treatment systems, such as phone or web-based interventions are currently in development for addiction treatment, including office-based buprenorphine (Bup). Provider acceptability and expected utility of these systems has not been evaluated.
Methods: We conducted an anonymous, 15-minute, Web-based survey through SurveyMonkey. Approximately 7000 Bup prescribers and members of an addiction medicine society were sent an introductory email and link.
Results: 454 individuals initiated and 346 (76%) completed the survey. 55% of providers rated a model automated system as "very" or "extremely" interesting. The primary uses were for "immediate cravings"(80%) and "when other services are not available"(76%), and the most important features were "24 hour access"(82%) and "information about dealing with cravings"(86%). Primary perceived barriers were "patient access and hesitancy with technology"(60%) and "lack of patient interest"(62%). Providers expected that 50% of patients would benefit, and predicted patients would use the system more than once per month. Providers predicted implementing a system only if covered by insurance (M = 3.6 of 5), and estimated such a service would be worth $70/patient/month. Primary specialization of addiction medicine or psychiatry (AMP, 53%), was compared to internal medicine, family practice, or other medical focused practice (IMFP, 47%). AMP providers were more likely to offer counseling, while IMFP providers were more likely to refer ($p<.001$). IMFP providers rated patient likelihood of use and expected frequency of patient use ($p=.02$) higher than AMP providers. Provider specialization was not associated with patient characteristics, perceived barriers, willingness to pay, or preferred billing options for an automated system.
Conclusions: Bup providers report interest in automated systems to provide ancillary service and believe patients would benefit and use the system. IMFP providers expect greater benefits of an automated system than AMP providers.
Financial Support: NIDA K01DA022398, R01DA019511

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"THIS IS NOT WHO I WANT TO BE:" EXPERIENCES OF OPIOID-DEPENDENT YOUTH PRIOR TO, AND DURING, COMBINED BUPRENORPHINE AND BEHAVIORAL TREATMENT.

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Aims: This study collected novel qualitative data from youth in treatment for opioid dependence regarding their experiences with both opioid dependence and combined behavioral-pharmacological treatment for opioid dependence.
Methods: Youth participants were recruited from a larger randomized controlled trial examining the relative effectiveness of two tapers of buprenorphine-naloxone for youth (eligible ages 13-24). Twenty-two youth participated in 1-1.5-hour semi-structured interviews. A grounded theory approach influenced the analysis.
Results: Mounting unintended consequences and increasing isolation pervade descriptions of opioid dependence among youth. To describe reaching the point where they needed help, youth highlight momentary glimpses of the dependent self and struggles to envision that self in the future. Descriptions of treatment experiences emphasize the effectiveness of buprenorphine and voucher-based reinforcement of negative urines, and the importance of engagement with staff.
Conclusions: These results have the potential to inform the development of efficacious treatments for this growing, yet understudied, group of youth.
Financial Support: NIDA Grant #1R01 DA018297

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ASK YOUR MOTHER: PARENTAL REPORTS ON ADHD, LIFE STRESS AND FAMILY HISTORY OF ALCOHOL ABUSE.

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Aims: Aims: Prevalence of ADHD in children ages 4-17 ranges from 6-16% (CDC). While a number of risk factors have been identified (e.g., genetic risk, neuropsychological vulnerability, etc.), the etiology of ADHD remains unclear. One prominent risk factor is parental substance use (Wilens et al, 2005). The present study examined the relationship between family history of alcoholism, family life stressors and symptoms of ADHD in a sample of children attending an urban pediatric clinic.
Methods: Methods: Study participants were 155 biological parents of children seeking pediatric care. Participants completed a brief research interview with measures of demographics, family stressors (Life Stresses Scale), parental and grandparent SUDs (Family Alcohol Drug Scale) and child behavior problems (Vanderbilt). Families were categorized as FHP (alcoholism in 1+ parents and/or grandparents) or FHN (no alcoholism in parents/grandparents). Children were identified by parents for ADHD diagnosis (presence/absent). Comparison was conducted using bivariate correlation.
Results: Results: Demographically, participants were primarily female (93%), African-American (90%), and never married (64%), with a mean age of 33 years (SD=6.5). Correlation results found that ADHD and higher rates of life stress are positively correlated ($r=.164$, $p<.05$). Also, a family diagnosis of a SUD and a child with ADHD showed a small, but significant, positive correlation ($r=.191$, $p<.05$). Additional analysis of variance showed paternal drug use as a significant predictor of an ADHD diagnosis (3%, $p<.05$) as was grandparent substance use (6%, $p<.01$).
Conclusions: Conclusions: Study findings continue to support a relationship between parental substance use and family stressors contributing to child attentional problems. Further research should look to identify additional environmental factors contributing to the development of attention problems.
Financial Support: Financial Support: NIDA R03 DA023563-01, NIDA award R01DA026091

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DIFFERENTIATING THE ASSOCIATION BETWEEN CIGARETTE SMOKING AND METHAMPHETAMINE USE ON GRAY MATTER ABNORMALITIES SEEN IN METHAMPHETAMINE ABUSERS.

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Aims: As most methamphetamine (MA) abusers also smoke cigarettes, smoking may contribute to gray matter (GM) abnormalities in this population. We compared the effects of cigarette smoking, alone and in combination with MA abuse, on gray matter structure.
Methods: We measured GM intensity throughout the brain (voxel-based morphometry) and GM volume of striatal nuclei with a semi-automated tool for tracing regions of interest (FSL-FIRST). 18 nonsmokers, 29 smokers, and 40 MA-dependent smokers free of Axis I psychiatric disorders except for MA dependence and nicotine abuse or dependence participated in the study.
Results: GM intensity differed across the groups in bilateral frontal and temporal cortices, right parietal and left limbic cortices ($p<0.05$, FDR corrected). Compared with nonsmokers, both cigarette smokers and MA-dependent smokers had deficits in these brain regions ($p<0.05$, FDR corrected). MA-dependent smokers also had smaller caudate volumes than nonsmokers ($p<0.05$ Bonferroni corrected). Compared with smokers, however, MA-dependent smokers exhibited notable deficits in subregions temporal and frontal cortices (~8%; $p<0.05$ FDR corrected), but we failed to detect added effects of MA in many subregions where there were differences among the three groups.
Conclusions: Gray matter abnormalities associated with tobacco smoking contribute to a large portion of the structural brain abnormalities observed in methamphetamine-dependent individuals. These abnormalities occur in brain regions that are important in cognitive control and reward that may influence drug dependence and the efficacy of treatments for addiction.
Financial Support: NIH research grants R01 DA020726, R01 DA015179, P20 DA022539, M01 RR00865 (UCLA GCRC), endowments from the Katherine K. and Thomas P. Pike Chair in Addiction Studies and the Marjorie Green Family Trust (EDL) and NIH grant T90-DA022768.

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MOTIVES ASSOCIATED WITH CONSUMPTION OF ALCOHOL 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 consumption of alcohol in school students in Spain, analyzing differences by gender.
Methods: The sample is 991 students, 46,5% (n = 461) male, mean age 15,28 (SD=3.33). Was given a "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; administered in 21 schools in the Valencia City. It was applied Chi-square test, to determine differences by gender in three groups: only have proved it, occasional consumption and daily consumption.
Results: In males and females, the main motives for consumption are: "to have fun" (49,7% males; 50,4% females); "to experience new sensations" (30,2% males; 32,5% females); and "for anything in particular" (28,6% males; 33,6% females). Among those who answer to consume occasionally (e.g. weekends), the motive "to maintain sexual relations" was answered in more proportion by males ($X2=8,8$; $p<.01$); and was answered in more proportion by females the motives "to forget my problems" ($X2=5,3$; $p<.05$), and "for anything in particular" ($X2=7,3$; $p<.01$). Among those who answer that only proved the alcohol, or have daily consumption, there are no differences by gender in the motives.
Conclusions: To have fun and experiment new sensations are the principal motives for alcohol consumption. Gender differences regard the motives for consumption it appear especially among students that consume ocassionally: with females consuming more to forget own problems and for nothing in particular; and males more in order to maintain sexual relations.
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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SEX DIFFERENCES IN BRAIN ACTIVITY FOLLOWING CORTICOTROPIN-RELEASING HORMONE IN COCAINE-DEPENDENT MEN AND WOMEN.

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Aims: The stress hormone corticotropin releasing hormone (CRH) has been implicated in drug seeking behavior. Specifically, plasticity within extrahypothalamic CRH sensitive nuclei as a consequence of long-term drug use has been hypothesized to promote drug craving and relapse. In agreement, CRH has been shown to produce drug craving in cocaine dependent men and women, yet women may be more susceptible to relapse following stress than men. The purpose of the study was to use pharmacological fMRI to compare brain activity following saline and CRH administration between cocaine-dependent men and women.
Methods: Cocaine-dependent men (n=10) and women (n=8) were placed in a Siemens Trio 3T scanner. Subjects received i.v. saline followed by CRH (1 ug/kg) and remained in a wakeful rest state during each 12 minute scan. Stress and craving ratings were obtained every two minutes. Data were normalized to baseline and regions of interest (ROI) included bilateral amygdala, caudate, insula, anterior and posterior cingulate cortices.
Results: Cocaine dependent women reported significantly ($p<0.05$) greater stress during the placebo and CRH scans than men. CRH attenuated activity in the left amygdala, left and right anterior cingulate cortices, left and right caudate, left and right insula, left and right posterior cingulate cortices. Significant gender by time interactions were found, with women exhibiting significantly less activity than men in the following ROIs; left and right anterior cingulate cortices, left and right caudate nuclei, left and right insula.
Conclusions: These data indicate that CRH attenuates brain activity in extrahypothalamic nuclei associated with long-term drug use and relapse. Furthermore, these data add to a growing literature demonstrating sex differences in the neurobiological substrates of substance dependence.
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ADHERENCE TO CLINICAL GUIDELINES FOR OPIOID THERAPY FOR CHRONIC PAIN IN PATIENTS WITH SUBSTANCE USE DISORDER.

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Aims: Patients with chronic non-cancer pain (CNCP) have high rates of substance use disorders (SUD). There is little information about adherence to opioid treatment guidelines for CNCP generally, and no data about adherence among patients with comorbid SUD. We sought to examine adherence to opioid treatment guidelines based on SUD status.
Methods: Electronic medical record data were collected from veterans with CNCP receiving treatment within a VA regional healthcare network who were prescribed chronic opioid therapy (n=5814). A 2008 index date was selected for each patient based on receiving prescriptions for opioids for 90 or more consecutive days. Medical utilization data were collected for the subsequent 12 months after the index date.
Results: Twenty percent of CNCP patients prescribed chronic opioid therapy had a past-year SUD diagnosis. Significant differences existed between veterans with and without a past-year SUD diagnosis on demographic characteristics, pain diagnoses, and psychiatric comorbidity. After controlling for demographics and clinical factors, patients with a past-year SUD diagnosis were more likely to have had a mental health therapy session (OR=1.49, 95% CI=1.26–1.77) and to have been administered a urine drug screen (UDS) (OR=3.53, 95% CI=3.06–4.06). There were no significant differences between the groups on other treatment guideline indicators, including more intensive treatment in primary care, receiving long-acting opioids, participating in physical therapy, or receiving prescriptions for antidepressants.
Conclusions: CNCP patients with comorbid SUDs who are prescribed opioids long-term are more likely to participate in mental health therapy and receive UDS monitoring. They are no more likely than patients without past-year SUD diagnoses to receive other pain care. Given data suggesting patients with comorbid SUD need more intensive treatment to achieve improvements in pain-related function, they are at risk for poor outcomes.
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CAFFEINE ACTIVATION OF BRAIN STRESS REGIONS.

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Aims: Caffeine is the most widely consumed psychoactive stimulant in the world, due in part to its wake-promoting properties. However, at high doses, or in individuals particularly sensitive to its effects, caffeine may cause anxiety and nervousness. Research has focused on determining caffeine's effects on limbic brain regions such as the amygdala, which coordinates emotional, behavioral and endocrine components of anxiety responses. Caffeine's pharmacological interaction with the amygdala is hypothesized to mimic the body's cellular reactions to stress and stressful experiences. In this study, we examine the impact of acute caffeine administration on the basolateral amygdala (BLA) in rats using the immediate-early gene, cfos, as a marker for neuronal activation.
Methods: Three different groups of adult male rats were given acute caffeine injections of 0.0 (vehicle), 10 (low), or 50 (high) mg/kg intraperitoneally. Brains were harvested two hours after acute drug administration to ensure optimal cfos expression. Immunohistochemistry assays used cfos to visualize general neuronal activity. Marker proteins calbindin (CB) and calretinin (CR), were used to double-label GABAergic inhibitory interneurons in the BLA. Cell counts were evaluated using an observer-blind procedure.
Results: The results indicated a significant increase in single-labeled cfos expression for low and high dose groups. Activated cfos cell populations in the 10 and 50 mg/kg groups also had significant increases in cells double labeled for cfos and CR or CB, compared to controls. In the 10 and 50 mg/kg groups, 26.45% and 22.09% of cells were double-labeled for CB and cfos, respectively. For CR labeled cells, the low-dose group had an average of 1.8% double-labeling for cfos, and 2.5% double-labeling in the high-dose group.
Conclusions: These results confirm the hypothesis that acute caffeine administration activates neuronal populations in the basolateral amygdala, similar to those activated during the
biological stress response.
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BEHAVIORAL AND NEUROCOGNITIVE EFFECTS OF LOW, ESCALATING DOSES OF METHAMPHETAMINE ADMINISTRATION.

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Aims: Methamphetamine is a psychoactive stimulant drug with effects characterized as an increase in alertness, energy, and euphoria, and is a drug of abuse that has gained popularity over the past several decades. Research from our laboratory (e.g. Kobeissy et al., 2008; Gold et al., 2009) has shown that high doses or chronic administration of methamphetamine can cause long-lasting (perhaps permanent) brain changes associated with neurotoxicity. It was the goal of this investigation to develop a dosing regimen that mimics particular aspects of human drug use (e.g. increasing dose and frequency of administration over time), examine neurobiological changes and potential neurotoxicity, and to characterize various behavioral and neurocognitive consequences.
Methods: Male, Sprague-Dawley rats (n=16) were administered methamphetamine (or saline) in a dosing regimen patterned to gradually increase the dose and frequency of administration over time. Locomotor activity (a behavioral indication of psychostimulant action) and performance in the Morris water maze (a cognitive behavioral task sensitive to hippocampal function) were examined.
Results: Assessment of locomotor activity revealed a biphasic dose-response curve (i.e. low doses increase and high doses result in lower levels of locomotor activity). Repeated administration of low doses resulted in a sensitization-like increase in activity over time (~150% of initial locomotor stimulation elicited by 1.0 mg/kg). Locomotor sensitization was also apparent following a 2-week period of chronic administration. Methamphetamine had no considerable effect on behavior in the Morris water maze (5 blocks of 3 trials within one session, followed by a 24-hr "probe" trial).
Conclusions: Taken together, these data show that low, but escalating doses of methamphetamine can produce profound behavioral effects. This dosing regimen may have greater behavioral relevance to human drug users compared to acute or short duration, high dose regimens optimized for producing neurotoxicity.
Financial Support: These experiments were supported by institutional funds.

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SUBSTANCES, ACADEMICS, AND COLLEGE STUDENT GOALS.

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Aims: To conduct an analysis of harm reduction goals among struggling college students Data came from a study showing that students who participated in a goal-setting program had significantly reduced negative affect and improved academic performance. In re-approaching the data, we hypothesized that several participants set goals for reduced substance use and that these goals contributed to the positive outcomes. Substance abusers are often unclear about long-term goals. A disconnect occurs between current behavior and future success without goal articulation. About 25% of students report academic consequences of substance abuse Individuals with clear goals are more able to direct attention toward goal-relevant activities and away from goal-interfering activities. A BI that helps students articulate goals may direct attention toward goal-precipitating behaviors and away from goal-interfering behaviors
Methods: Descriptive analyses were used to determine the number of students who reported a desire to change substance use; qualitative analyses were used to characterize the substance use goals and the individuals who set them.
Results: Of the 8 students (of 45) who reported a desire to change their substance use, 87.5% were female; ethnicity was broadly distributed. They were skewed towards a higher SES than students without substance goals. They were further compared on baseline measures of personality, depressive symptoms, perceived stress, and neurocognition.
Conclusions: BIs for substance use in college students are a prime target for investigations. The substance goals among our participants were not program prompted, and suggest that for struggling students, altering substance use is tied to future-oriented thinking. Participants who identified substance use goals placed them in a broad context, relating reduced use to improved school habits and a healthier lifestyle. Goal-setting, as an intervention, may have promise for this population.
Financial Support: McGill Internal Grant

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UNDERSTANDING DRUG USE TRAJECTORIES LEADING TO INJECTION INITIATION AMONG FEMALE SEX WORKERS WHO INJECT DRUGS.

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Aims: We studied relationships between behavioral, social, and economic factors associated with the rate of transition into injection drug use among FSW-IDUs.
Methods: Analyses were carried out using baseline data on 566 FSW-IDUs ≥ 18 years old living in Tijuana or Ciudad Juarez who reported injecting drugs and recent unprotected sex with clients participated in a longitudinal behavioral intervention. Cox proportional hazards models of time to injection drug initiation were created to identify factors associated with differences in duration from first illicit drug use to first injection drug use, overall and by city.
Results: Overall, median age was 33 years, median age of first illicit drug use other than marijuana was 16 years (IQR: 14-20), and median age of first injection was 20 years (IQR: 17-26); 26% reported initiating both non-injection and injection drug use within the same year, and 3 reported initiating injection drug use prior to illicit drug use. In bivariate analyses, we found experiencing rape, abuse and initiating sex work earlier to be associated with shorter trajectories. Further, FSW-IDU who began selling sex to pay for drugs had significantly shorter trajectories. Conversely, living in a greater number of cities extended the duration. After adjusting for age and number of drugs used, a multivariate proportional hazards model indicated that beginning sex work earlier (Hazard rations [HR] per year increase:0.98, 95% CL:0.95-0.98); initiating non-injection drug use with cocaine (HR:1.45, CL:1.1-1.9); ever being raped (HR:1.23, CL:1.0-1.5); and living in Ciudad Juarez (HR:1.27, CL:1.1-1.6) all accelerated the rate from first illicit drug use to injection.
Conclusions: Exposure to abuse, rape, and early entry into the sex trade were associated with accelerated trajectories to injection drug use among FSWs. Understanding how these life-altering events shape substance use experiences will contribute to improved interventions.
Financial Support: NIDA grant: DA023877

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MDMA (ECSTASY) USE IS ASSOCIATED WITH INCREASED AMYGDALAR AND HIPPOCAMPAL ACTIVATION DURING NOVELTY DETECTION.

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Aims: Recreational use of MDMA, a serotonin neurotoxin, has been associated with increased anxiety. The amygdala and hippocampus are involved in the genesis of anxiety and are innervated by serotonin. Brain response to novel situations or stimuli can elicit anxiety. We used fMRI BOLD along with a novelty exposure paradigm to compare amygdala/hippocampal activation to novelty in MDMA users and controls.
Methods: We enrolled 16 abstinent MDMA users and 16 controls with no history of DSM-IV mood or anxiety disorders. We used a block design to test amygdala and hippocampal BOLD responses to three types of images: Familiar (common images shown during an initial familiarization phase), Novel Common (common but novel in the context of the scanner), and Novel Uncommon (unlikely to have been seen before in any context). SPM5 was used for data analysis. Statistical thresholds were corrected for multiple comparisons. A linear regression analysis was performed for MDMA lifetime use versus amygdala and hippocampus BOLD signal intensity change.
Results: MDMA users had a larger increase in BOLD signal than controls for the following contrasts: Novel Common>Familiar in both the amygdala (left: p=.02; right: p=.01) and hippocampus (left: p=.01, right: p=.02), Novel Uncommon>Familiar for the left hippocampus (p=.02), and Familiar>Baseline contrast in the left hippocampus (p=.02). For the Novel Uncommon>Novel Common contrast, controls had greater right amygdala activation than MDMA users (p=.02), as did the hippocampus (L: p=.02; R: p=.03). Lifetime MDMA use was positively correlated with BOLD signal intensity for the Novel Common>Familiar contrast (r=.52, p=.04) and the Novel Uncommon>Familiar contrast (r=.58, p=.02) in the right amygdala.
Conclusions: Thus, amygdala and hippocampal neurophysiology are likely altered in MDMA users. The fMRI BOLD method may be sensitive to MDMA neurotoxicity that is subthreshold for producing detectable mood or anxiety changes.
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SYNTHESIS AND OPTIMIZATION OF SELECTIVE N-PHENYLETHYL PIPERAZINE ANALOGUES AS SIGMA-2 RECEPTOR ANTAGONISTS.

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Aims: Drugs that have the capability to suppress the psychostimulant activities of methamphetamine are highly sought after technologies, yet little success has been achieved due to the number of receptors with which the substance interacts. It has been shown that selective sigma receptor antagonists attenuate many of the stimulant (σ) and neurotoxic (σ2) effects of methamphetamine, indicating that drug development aimed specifically at sigma receptors has the potential to yield an effective treatment for the stimulant and neurotoxic effects of methamphetamine. A series of compounds has been developed that have shown mixed antagonism of sigma-1 and sigma-2, reversing both the stimulant and neurotoxic effects. The aim of this project is to optimize previously synthesized drugs to enhance the σ2 selectivity of potential antagonists to determine the contributions from σ2.
Methods: Analogs of UMB24, a selective σ2 ligand, were synthesized to determine the influence of the pyridine ring, and binding affinities were determined in rat liver for σ2 and guinea pig brain for σ1. Radioligand binding assays were performed to determine receptor subtype selectivity. Molecular modeling was performed using the conformationally sampled pharmacophore approach.
Results: UMB 93 possessed a non-basic nitrogen in the 4-position of the piperazine and had binding affinities of 20 ± 14 (nM) for σ1 and 180 ± 15 for σ2, while UMB 226 lacked a heteroatom at the 4-position and had binding affinities of 3.3 ± 0.4 (nM) for σ1 and 120 ± 2.6 for σ2.. This result indicates that both compounds showed σ1 selectivity.
Conclusions: These studies demonstrate that the heteroatom and the non-basic nitrogen of the piperazine ring of UMB24 are essential for σ2 selectivity. Further studies will be conducted to examine the effect that the orientation of the pyridine group has on selectivity.
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EDUCATION AND REINFORCING EFFICACY OF CIGARETTES PREDICT RATES OF DELAY DISCOUNTING AMONG SMOKERS.

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Aims: Delay discounting is known to be a behavioral marker of drug addiction. However, variability in this measure in smokers prevents a comprehensive understanding of the factors that maintain smoking. Data from measures related to both smoking and delay discounting will enhance our understanding.
Methods: 93 smokers completed delay-discounting assessments of hypothetical monetary gains of $10 and $1000 and of hypothetical cigarette gains subjectively deemed equivalent to $10 and $1000, and also various assessments related to degree of smoking. The assessments, as well as demographic variables, were entered into multivariate regressions in a step-wise fashion to identify predictors of delay discounting.
Results: Years of education and reinforcing efficacy of cigarettes predicted discounting rates. Generally, increased education corresponded with decreases in discounting ($p=.043$); however, the decreases depended on both the commodity (money or cigarettes; $p=.038$) and amount ($10 or $1000; $p=.020$). For reinforcing efficacy, increases corresponded with increased discounting ($p<.001$), irrespective of commodity or amount.
Conclusions: The direction of relations in these data support the interpretation of smoking as a phenomenon reflective of competing neurobehavioral brain systems. Higher education achievement levels and lower delay discounting rates are proposed to result from the functioning of the executive system in the brain, while higher discounting rates and higher measures of reinforcing efficacy are proposed to result from the functioning of the impulsive system in the brain.
Financial Support: This work was funded by NIDA grants R37 DA006525 and 5R01 DA022386

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GENDER DIFFERENCES IN METHADONE-MAINTAINED COCAINE USERS.

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Aims: Gender plays a crucial role in treatment efficacy for substance dependence, however there is limited data on the specific needs of substance dependent women. This is partially due to the numerous societal and psychological barriers that not only prevent women entry into treatment programs, but force them to avoid seeking treatment. Uncovering these basic differences will allow researchers to develop programs tailored to the specific needs of women.
Methods: We reviewed a 24-week double blind, placebo-controlled trial that evaluated the efficacy of a cocaine vaccine. Although the primary focus of the trial was on cocaine abstinence, it provided an opportunity to examine potential gender differences in the specified population. Cocaine and opioid dependent participants were recruited (n=115, 23% female, aged 18-46). Methadone-maintained subjects were studied because of the higher retention rates in methadone maintenance programs.
Results: Both genders had a majority of white (male=80%, female= 95%) and never married (male=71%,female=58%) subjects. In addition, both genders used heroin as their primary drug of use (male=84%, female=76%) and cocaine as their secondary drug of use (male=91%, female=84%). However, 53% of women lived with their children compared to only 16% of men. Additionally, there was a significantly higher number of women whose spouse or mates also use drugs (55%) compared to (15%) of men. Regarding employment, the majority of women were unemployed (55%), while the majority of men were either unemployed (40%) or full time employed (40%). Consistent with a more rapid trajectory to dependence, women reported a later onset (female=23 vs. male=20), but fewer years (male=14 vs. female=11) of cocaine use prior to seeking treatment. While treatment outcome for cocaine did not differ across gender, women submitted significantly fewer opiate positive urinalysis ($F=7.9$; $p=.006$).
Conclusions: Taking into account these gender differences will facilitate the development of gender-specific treatment programs that in the future will promote the enrollment and retention of women.
Financial Support: NIDAR01-DA15477

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IN VIVO EVIDENCE FOR LOWER STRIATAL VESICULAR MONOAMINE TRANSPORTER IN COCAINE ABUSERS.

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Aims: PET studies in cocaine abusers (CA) have shown that lower dopamine transmission in the striatum following a psychostimulant challenge is associated with relapse to cocaine. A possible mechanism that leads to lower dopamine transmission may be related to the available VMAT2, which regulates the size of the vesicular dopamine pool that is available for release, by stimulants. Consistent with this postmortem studies have reported lower VMAT2 availability in CA relative to healthy controls (HC). Here, we used PET and the VMAT2 radioligand [11C]-(+)-dihydrotetrabenazine (DTBZ) to assess the in vivo VMAT2 availability in CA to confirm the postmortem findings.
Methods: 12 cocaine abusers (CA) and 12 matched HC subjects were recruited. All CA were monitored for abstinence for a minimum of two weeks before they received the scans. [11C]DTBZ binding potential (BPND) was measured in the three functional subdivisions of the striatum (limbic, LST, associative, AST and sensorimotor striatum SMST, as defined in Martinez 2003) with kinetic analysis using the arterial input function (20/24 subjects) and the simplified reference tissue method (4/24).
Results: No significant between-group differences were observed in [11C]DTBZ occipital cortex distribution volume. A repeated measures ANOVA demonstrated that CA had significantly lower [11C]DTBZ BPND in the striatal subdivisions relative to HC (region factor: $p < 0.0001$; group factor: $p < 0.0001$; group-by-region interaction: $p = 0.14$). [11C]DTBZ BPND was significantly lower by 10% in the LST, 16.3% in the AST, and 13.4% in the SMST in CA compared to HC
Conclusions: This study confirms in vitro reports of a decrease in VMAT2 availability in the striatum of CA. It also suggests a compensatory downregulation of the dopamine storage vesicles in response to chronic cocaine abuse and/or a loss of dopamine terminals. Further research is necessary to understand the clinical relevance of this finding as to whether it is related to relapse in abstinent CA.
Financial Support: NIDA, ARRA and NCRR/CTSA

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GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO CANNABIS WITHDRAWAL AND ABUSE/DEPENDENCE IN A NATIONAL ADULT TWIN SAMPLE.

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Aims: No published study to date has examined the genetic and environmental influences on cannabis withdrawal. The objectives of the current study were to (a) estimate the heritability of withdrawal and (b) test for common or specific genetic pathways between cannabis abuse/dependence symptomatology and withdrawal.
Methods: Symptoms of cannabis withdrawal and abuse/dependence were assessed in a sample of 3915 adult male and female Australian twins. Cannabis withdrawal was defined in accordance with DSM V and abuse/dependence problems was defined as endorsing one or more DSM IV criteria of abuse/dependence, excluding the legal problems criterion. A bivariate ACE model using the Cholesky decomposition was used to estimate the genetic and environmental parameters.
Results: The most parsimonious and best fitting bivariate model estimated that, for both males and females, 70% of the variance in withdrawal could be attributed to additive genetic factors, and 30% to non-shared environmental factors. Furthermore, the model estimated that, for both males and females, 65% of the variance in cannabis abuse/dependence symptoms could be attributed to additive genetic factors, and 35% to non-shared environmental factors. We found no shared environmental influence for both phenotypes. Importantly, there was no evidence for genetic influences on cannabis withdrawal that did not overlap with other abuse/dependence symptoms.
Conclusions: Contrary to our expectations, we did not find specific or stronger genetic influence on cannabis withdrawal compared to abuse/dependence, suggesting a common genetic route for withdrawal and abuse/dependence.
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ACTIVATION OF THE CORTICOTROPIN-RELEASING FACTOR SYSTEM IN THE AMYGDALA IS RESPONSIBLE FOR THE REINSTATEMENT OF METHAMPHETAMINE-SEEKING BEHAVIOR INDUCED BY FOOTSHOCK STRESS.

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Aims: Corticotropin-releasing factor (CRF), which serves as a stress hormone, is indicated to be involved in the reward system. This study investigated the role of CRF in reinstatement of methamphetamine (METH)-seeking behavior induced by footshock stress.

Methods: Rats were trained to lever-press for intravenous METH (0.02 mg/0.1 ml per infusion, i.v.) accompanied by light and tone (drug-associated cue; cue) using a self-administration paradigm and then underwent extinction training (saline substituted for METH without cue). Reinstatement behavior following footshock (0.8 mA, 15 min) was tested under extinction condition and brain/plasma CRF levels were measured during METH withdrawal.

Results: The non-selective CRF receptor antagonist α-helical CRF_{9-41} (30 μg/side, i.c.v.), attenuated METH-seeking behavior. The CRF level in the amygdala but not that in the nucleus accumbens and hypothalamus was significantly increased on withdrawal day 10 after METH self-administration. Although the level of plasma CRF was also increased at that time, plasma corticosterone was not changed. However, METH-seeking behavior was not affected by the corticosterone synthesis inhibitor, metyrapone (100 mg/kg, i.p.). In the elevated plus maze test, METH self-administered rats spent significantly less time in the open arm on withdrawal day 10 without any change in the number of crossings.

Conclusions: The present findings indicate that increased CRF release in the amygdala may, at least in part, play a facilitating role in the reinstatement of METH-seeking behaviors following footshock and the elevation of anxiety-like behavior without participation in corticosterone. Furthermore, CRF receptor antagonist may be useful as an anti-craving agent and plasma CRF may have potential as a diagnostic biomarker for measuring the craving risk in METH abusers.

Financial Support: This study was supported by a grant from the Ministry of Health, Labor, and Welfare of Japan.

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INCREASED SENSITIVITY OF FEMALE C57BL6 MICE TO PACLITAXEL-INDUCED NEUROPATHIC PAIN AND PLACE-CONDITIONING.

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Aims: Behavioral studies using rodent models of Paclitaxel (PAC), a chemotherapy-induced neuropathic pain (CINP) state are largely restricted to male rats while well-characterized effects of CINP in female mice, although more relevant, are lacking. In the present set of experiments, we investigated: i) PAC-induced neuropathic pain, ii) effect of CBD on PAC–induced allodynia in female C57Bl/6 mice, and iii) sensitivity of the PAC treated mice to either morphine or CBD place conditioning effects.

Methods: We investigated the effect of a wide range of repeated PAC doses (1.0 – 8.0 x 4 inj IP) on cold and mechanical allodynia using acetone drop test and Von Frey test in male and female C57Bl/6 mice. We assessed the effect of cannabidiol (CBD; 5.0-10.0 mg/kg IP) treatment on PAC-induced cold and mechanical allodynia in the female mice using the above two mentioned assays. Further, using two separate place conditioning procedures: pseudo-biased model and single-pairing procedure, we evaluated the sensitivity of the PAC treated mice to either morphine or CBD place conditioning effects, respectively.

Results: Treatment with PAC led to the onset of cold and mechanical allodynia in male and female mice after approximately 10 days post treatment. These effects were largely dose-independent, with some effects larger in females than males. Both doses of CBD produced a statistically significant blockade of the development of PAC-induced cold and mechanical allodynia. PAC-treated mice showed an enhanced morphine place preference and an increased time spent in a CBD-paired chamber compared with saline treated mice.

Conclusions: Taken together, these results demonstrate that paclitaxel induces neuropathic pain in the female C57Bl6 mice that is prevented by concomitant treatment with CBD and that place-conditioning procedures provide as an additional tool to indirectly measure neuropathic pain and antinocicpetion.

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SPIRITUAL AND RELIGIOUS BELIEFS AND BEHAVIORS, SELF-HELP PARTICIPATION AND OPIOID USE.

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Aims: Spirituality and religiosity are associated with recovery from substance abuse disorders, but specifics of the relationships among spiritual/religious beliefs and behaviors and recovery have not been closely examined. The current study addresses spiritual/religious beliefs and behaviors in opioid-dependent individuals.

Methods: 123 study participants who completed 16 weeks of combined pharmacotherapy with buprenorphine and behavioral treatment in an ongoing trial were assessed at baseline and at end of the treatment period. Participants were distinguished by endorsement of the statement "I look to God for strength, support, and guidance" with analyses using only the extreme responses of "not at all" (-God, n = 31, 25.5%) and "a great deal" (+God, n = 37, 30.1%).

Results: Baseline group differences were found for age and gender with the +God group significantly older with a greater percentage of females. Group differences were also found for other spiritual/religious beliefs and behaviors including having prayed in the past year ($p < 0.00$), and participants' belief that there is a real purpose for their lives ($p < 0.00$). No significant difference between the groups was found regarding 12-Step group attendance in the 6 months prior to treatment. Other findings will be reported including changes in spiritual/religious beliefs and behaviors from baseline to end of treatment, and associations among 12-Step group attendance, spirituality, and opioid use.

Conclusions: Study findings support previous research showing associations among spiritual beliefs/behaviors, self-reported substance abuse, and recovery activities, and suggests that further research should address specific components of spirituality/religiosity.

Financial Support: NIDA (DA020210)

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TOWAR: A COMPREHENSIVE TRAINING ON WOMEN'S ADDICTION AND RECOVERY FOR DRUG COURTS.

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Aims: While innovations in existing drug courts are helping to reduce drug use and recidivism, few programs are designed to meet the complex needs of female offenders and outcome studies are typically relative to male drug court participants. Recent studies have found that women entering drug court treatment programs are at a substantial disadvantage compared with their male counterparts and are more likely to present greater challenges to treatment practitioners. With funding from NIDA, Social Solutions International in collaboration with UCLA ISAP is developing a training and woman-focused model of care for drug court programs.

TOWAR has the following aims: 1) to develop a woman-focused training program to educate drug court personnel on specific issues relevant to the recovery of drug-dependent women offenders; 2) to develop a drug court model of care for drug-dependent women offenders; and 3) to qualitatively assess the feasibility of a woman-focused drug court model of treatment.

This presentation will describe the development of the TOWAR training and model of care, to include expert panel feedback, and will outline results of a pilot test with drug court personnel to determine the acceptability, feasibility, and perceived value of the program.

Conclusions: The objective of the feasibility study was to determine: 1) whether the training and woman-specific drug court model of care provided materials and guidelines useful and appropriate to the target audience; and 2) the feasibility of implementing the TOWAR Toolkit in a drug court setting. At the completion of the trainings, project staff asked participants to fill out evaluations. The evaluations captured data on participants' perceptions of the materials and guidelines usefulness and appropriateness. Each of the three trainings resulted in very positive feedback from the participants.

Financial Support: NIDA STTR# 1R41DA022101-01A2

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SEEKING ONLINE INFORMATION ABOUT DRUGS/ALCOHOL/TOBACCO BY JEWISH AND ARAB SCHOOLCHILDREN IN ISRAEL: WHO DOES, WHO DOESN'T AND WHO WANTS TO?

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Aims: Describe facilitators and barriers associated with seeking online drug/alcohol/tobacco information (DATI) and with an interest to obtain such information, among Jewish and Arab adolescents in Israel.
Methods: Information was collected via a standardized anonymous questionnaire from a nationally representative sample of 7,028 Jewish and Arab (Moslem, Christian, Druze and Bedouin) 7th-12th graders in 158 schools. First-order statistics compared outcomes (seeking online information and interest in online information) across religion and sex groups. Adjusted odds ratios (AOR) were derived from logistic regression models accounting for the complex sample design.
Results: Nearly two-thirds (62.7%) of Arab respondents and half (47.2%) of Jewish respondents sought health information online in the past-year; about 30% of boys and 23% of girls of both religions sought DATI in the past-year. The most common reasons for not seeking internet information among those interested in DATI were a preference for information from a health professional (Jews:79.1%, Arabs:55.0%), lack of trust in internet information (Jews:42.0%, Arabs:52.9%), and language barriers (Jews:23.3%, Arabs:42.5%). Amongst those who did not seek health information online, 42% and 39% of Jewish boys and girls, and 47% and 26% of Arab boys and girls, expressed interest in online DATI. For all religion-sex groups, the strongest correlates of wanting DATI were past-year drug use (AOR=3.2, 95%CI=1.7-6.1), alcohol drinking (AOR=2.1, 1.7-2.6) and smoking (AOR=2.7, 2.1-3.4).
Conclusions: An important proportion of Israel school age adolescents – Arabs and Jews alike, search for, or would like to receive, online information about drugs, alcohol, and tobacco, particularly those using them. This highlights the need for development of authoritative and user-friendly internet-based drug, alcohol and tobacco information and intervention sites in local languages.
Financial Support: Israel National Institute for Health Policy Research (YN and RS – Co-PIs).

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THE NORADRENERGIC α1 RECEPTOR ANTAGONIST DOXAZOSIN ATTENUATES COCAINE-INDUCED CRAVING IN NON-TREATMENT-SEEKING, COCAINE-DEPENDENT VOLUNTEERS.

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Aims: Genetic and pharmacological evidence has confirmed that noradrenergic mechanisms contribute to the reinforcing effects of cocaine and other addictive drugs. Doxazosin is an α1R antagonist with an elimination half-life of 22 hours that is indicated for the treatment of hypertension. We tested the impact of doxazosin treatment on the cocaine's effects in non-treatment-seeking, cocaine-dependent volunteers.
Methods: We used a within-subjects (N=9 to date, with 12 planned) design with study episodes separated by at least 2 weeks. Doxazosin treatment was started at 1mg/day and increased over 9 days to 4mg/day. Effects of cocaine (0, 20, 40mg, IV) were tested after 3 days of treatment with 4mg/day doxazosin/placebo.
Results: Doxazosin treatment was well tolerated. Doxazosin treatment was associated with reductions in "Desire Cocaine" and "Would Use Cocaine if Available" assessed using visual-analogue scales. There were also trends for doxazosin treatment to reduce other positive subjective effects of cocaine as well. Doxazosin treatment was well tolerated.
Conclusions: These results are consistent with earlier research showing that other medications such as disulfiram or SYN-117 that reduce noradrenergic signaling reduce the effects produced by cocaine. For example, disulfiram treatment attenuates the subjective effects of cocaine and reduces cocaine use. A newer drug with a similar mechanism of action, SYN-117, also reduces the positive subjective effects of cocaine. Both disulfiram and SYN-117 inhibit dopamine-β-hydroxylase, which mediates the conversion of DA into norepinephrine (NE), thus reducing the availability of NE for release. Our data are in keeping with the growing recognition of the role played by noradrenergic mechanisms in cocaine dependence.
Financial Support: P50 DA018197

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DEVELOPMENT OF TOLERANCE IN MICE DURING CARISOPRODOL TREATMENT.

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Aims: Carisoprodol, a muscle relaxant that is commonly prescribed for acute musculoskeletal conditions, has recently been recognized as a drug of abuse. The purpose of the current study was to determine if tolerance and withdrawal, factors that contribute to the development of abuse and addiction, were also associated with carisoprodol intake.
Methods: Carisoprodol (0, 100, 300, or 500 mg/kg bid) was administered to Swiss-Webster mice via intraperitoneal injection (i.p.), and the loss of righting reflex was measured 20 to 30 minutes following administration. Tolerance was inferred by a decrease in righting reflex impairment during the initial four days of exposure. Mice were assessed for signs of withdrawal, using rating scales sensitive to ethanol and barbiturate withdrawal, in two separate experiments, one testing spontaneous withdrawal, and one testing withdrawal precipitated by the antagonists bemegride or flumazenil.
Results: Swiss-Webster mice administered carisoprodol (300 mg/kg or greater i.p.) across 4 days exhibited a steady decrease in righting reflex impairment. A sudden loss of tolerance followed by death was observed in the mice beyond 4 days of carisoprodol administration. Mice treated with carisoprodol failed to exhibit withdrawal signs within 24 hours following chronic i.p. exposure alone; however animals administered bemegride or flumazenil exhibited signs of precipitated withdrawal 15 to 30 min following injection.
Conclusions: These studies indicate that regimens of carisoprodol treatment that result in the development of tolerance produce minimal spontaneous withdrawal; however, withdrawal could be precipitated by administration of barbiturate or benzodiazepine drug antagonists, suggesting barbiturate-like and benzodiazepine-like subjective effects from carisoprodol tolerance. These outcomes may be attributable to the relatively long half-life of the active carisoprodol metabolite, meprobamate.
Financial Support: NIH R01DA022370

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C-FOS AND AMPA RECEPTOR EXPRESSION FOLLOWING COCAINE CUE EXTINCTION LEARNING.

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Aims: Regional analyses of c-Fos protein expression and changes in GluR1 and GluR2 protein levels were used to delineate the neural activity and plasticity of AMPAR transmission associated with cocaine cue extinction learning.
Methods: Rats were trained to self-administer cocaine or received saline non-contingently. Infusions were paired with a 2 sec light cue under an FR5 schedule. Next, rats underwent either extinction training (EXT) where cocaine (n=21) or saline (n=20) infusions were withheld but response-contingent cues were presented or no-extinction training (No-EXT) where levers were retracted and cocaine (n=19) or saline (n=4) infusions as well as cues were withheld. Key brain areas were dissected from rats sacrificed immediately (GluR1 western blots) or 60 min (c-Fos and GluR2 immunohistochemistry) following completion of the 2 hr test session.
Results: Extinction learning was evident during the last 30 min of the test session; responding declined to 22 ± 7% of the cocaine self-administration baseline rate. c-Fos protein expression was selectively increased ($p<.05$) in the basolateral amygdala (BLA) after cocaine cue EXT relative to saline cue EXT (1.7-fold) and No-EXT (2.3-fold) controls. In prelimbic and infralimbic prefrontal cortex (PFC) and dorsal hippocampus subiculum, c-Fos levels following cocaine cue EXT were similar to saline cue EXT but greater than the No-EXT control ($p<.05$). GluR2 levels did not significantly differ amongst groups. Following cocaine cue EXT, GluR1 expression was increased in the nucleus accumbens (2-fold; $p<.05$) and reduced in the ventromedial PFC (0.5-fold; $p<.05$) and BLA (1-fold; $p<.05$) relative to No-EXT controls.
Conclusions: Based on c-Fos, there is a specific role for the BLA in cocaine cue extinction learning, whereas the subiculum and PFC may be involved in processing the salience of cues present during extinction training. Initial consolidation of cocaine cue extinction learning may be associated with internalization of the AMPA receptor in the BLA.
Financial Support: DA024315, Boston University Center for Neuroscience

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GENDER DIFFERENCES IN HEALTH AND PERCEPTIONS OF DRUG MISUSE AMONG PRESCRIPTION OPIOID MISUSERS.

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Aims: Prescription drug misuse is a growing problem in the US. This study examined health and perceptions related to prescription drug misuse by gender among a community-recruited sample of prescription opioid misusers in the St. Louis area.
Methods: The NIDA-funded Prescription Drug Misuse, Abuse and Dependence Study recruited and interviewed 349 prescription opioid misusers 18 to 65 years old. Misuse was defined as either using more or longer than prescribed or using someone else's prescription.
Results: The community-recruited sample of prescription opioid misusers was 44% female and 56% African American, with an average age of 39.1 (SD=12.8) years. Women were more likely than men to misuse their own prescribed opioids (78% vs. 53%, p<0.0001), while men were more likely to misuse someone else's prescribed opioids (79% vs. 66%, p=0.007). Among misusers, women were significantly more likely (p<0.05) than men to report high blood pressure, kidney infection, a weight problem, arthritis, a thyroid problem, and asthma, and were more likely to report that they were in poor health. Most misusers (75%) perceived prescription misuse to be more socially acceptable than illicit drug use; men were more likely to believe so (80% vs. 68%, p=0.017). Though most misusers felt safe using prescription drugs (78%), men were more likely than women to feel so (86% vs. 67%, p<0.0001). Finally, female misusers estimated the proportion of St. Louisans misusing prescription opioids to be higher than men's estimates (mean proportion 56% vs. 47%, p=0.003).
Conclusions: Among these prescription opioid misusers, women were more likely to misuse their own prescriptions and be in poor health. All were likely to misperceive the safety and acceptability of prescription drug misuse, with men even more likely to do so. Interventions should be tailored to address differing health needs and perceptions by gender.
Financial Support: This work supported by NIDA, R01DA020791, PI Linda B Cottler, PhD, MPH

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HYPERMETHYLATION OF SPECIFIC CPG DINUCLEOTIDES IN THE *OPRM1* GENE PROMOTER REGION IN RATS EXPOSED TO HEROIN.

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Aims: Previously, we showed that specific μ-opioid receptor gene (*OPRM1*) CpG dinucleotide sites are hypermethylated in leukocytes of methadone maintained former heroin addicts. Therefore, we hypothesized that heroin treatment of rats will cause hypermethylation of specific CpG dinucleotides in the *Oprm1* promoter region.
Methods: Rats were treated with either vehicle (N = 5) or heroin (N = 5), three times per day, every 4 h between 8:30 AM - 4:30 PM for seven days. Heroin intake was increased from 3.75 mg/kg to 30 mg/kg over the first five days, with the highest dose being repeated for three days. DNA was isolated from the ventral tegmental area/substantia nigra, ventral striatum, dorsal striatum, periaqueductal gray/hindbrain, frontal cortex, and blood. DNA methylation analysis of the *Oprm1* promoter region was performed by direct sequencing of bisulfite-treated DNA.
Results: *Oprm1* CpG dinucleotides were found to be hypermethylated in heroin treated rats. In the dorsal striatum, the *Oprm1* promoter region was hypermethylated overall in the heroin treated rats ($P = 0.037$).
Conclusions: Hypermethylation of the *Oprm1* promoter region in the dorsal striatum in response to heroin treatment may alter the expression of the μ-opioid receptor gene. This hypermethylation of the *Oprm1* promoter region is similar to our previous results in leukocytes of methadone maintained former heroin addicts. This study provides a model system to explore the mechanisms whereby opiates alter DNA methylation.
Financial Support: DA 020117

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BUPRENORPHINE INDUCTION OUTCOMES FOR HEROIN AND PRESCRIPTION OPIOID USERS.

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Aims: Many opioid-dependent people presenting for buprenorphine treatment are dependent on pharmaceutical opioid analgesics (POA). Despite this, little research has examined buprenorphine treatment in populations other than heroin users. Pharmacotherapy approaches used with heroin users may result in different outcomes when used with POA users. The aim of this secondary analysis was to examine buprenorphine induction and variations in outcomes according to opioid type (heroin vs POA).
Methods: Data for this analysis were from the first 175 buprenorphine inductions conducted in a current NIDA-funded study comparing behavioral treatments added to a platform of buprenorphine (Optimizing Buprenorphine, DA 020210). Participants were identified as either exclusive POA users or heroin users by self-report at screening. Analyses examined demographics, drug use and treatment history, and induction variables, including adverse events and withdrawal symptoms.
Results: POA users (n = 51) and heroin users (n = 124) differed on some demographic and drug use characteristics, including marital status and lifetime heroin use. Heroin users were clinically rated to have significantly higher pre-induction withdrawal (COWS) scores (p = 0.0.13). Post-induction COWS, self-reported craving, withdrawal scores and mean buprenorphine dose on day 1 did not differ between groups.
Conclusions: Some demographic and drug use differences are found between POA and heroin users, but induction outcomes appear comparable on many of the key variables including withdrawal, craving, and treatment retention. Existing buprenorphine induction practices developed for heroin users appear to be equally effective with POA users. Further research should explore possible associations between induction and other outcome variables.
Financial Support: Sponsored by The National Institute on Drug Abuse (R01 DA 020210). The first author is the recipient of a NIDA/CTN INVEST fellowship.

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DISCOVERY OF A NOVEL SSRI SCAFFOLD FROM A LEAD COMPOUND IDENTIFIED BY *IN SILICO* SCREENING.

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Aims: To identify structurally novel ligands for monoamine transporter (MAT) proteins by *in silico* screening. These compounds will serve as chemical leads for new CNS therapeutics and aid in characterizing MAT structure-activity relationships.
Methods: A 3-D computer model of the dopamine transporter (hDAT) was generated using the homolog LeuT crystal structure (2A65) as a template. This model was used to virtually screen a chemical database via docking with the Molecular Operating Environment (MOE) platform. Hit compounds were tested *in vitro* at the human dopamine, norepinephrine, and serotonin transporters (hSERT). Compounds passing an initial pharmacological screen (inhibition >50% at [10 μM]) were further assessed using radioligand displacement (K_i) and [^{3}H]-monoamine uptake inhibition assays (IC_{50}). Compounds having affinity (K_i <1.5 μM) for MATs were synthetically modified in an effort to define structure-activity relationships.
Results: Ten compounds from *in silico* screening were selected for pharmacological evaluation. MI-15, MI-17, and MI-20 had appreciable affinity for hDAT ranging from 801 nM to 1351 nM. Surprisingly, MI-17 showed better affinity towards hSERT than hDAT. Structural modification of MI-17 with an indole moiety resulted in increased affinity and selectivity for hSERT with no effect on hDAT.
Conclusions: Discovered through a virtual screening effort using hDAT, MI-17 was shown to have affinity for hSERT as well as hDAT. Incorporation of an indole group, a characteristic moiety of serotonin, into the structure of MI-17 significantly increased affinity and selectivity for hSERT. This study provides proof of concept that *in silico* screening of large chemical databases is a useful method for identifying new therapeutic lead compounds targeting MATs. Use of these compounds as novel leads for chemical exploration can further delineate the 3-D nature of MAT proteins.
Financial Support: R01DA026530, R01DA027806, P116Z050331 (DoE), P116Z080180 (DoE)

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PMS SYMPTOM SEVERITY AND DAILY CAFFEINE CONSUMPTION IN FEMALE COLLEGE STUDENTS.

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Aims: The relationship between caffeine consumption and symptoms of Premenstrual Syndrome (PMS) is complex. For the 40% of menstruating women who report some PMS symptoms, caffeine can both act as a diuretic (decreasing bloating) and elevate estrogen levels (exacerbating PMS symptoms. The present study compared PMS symptom type and severity in college women who did and did not drink coffee on a daily basis.
Methods: Participants were N=116 female undergraduate psychology students, 18 to 35 years of age, who completed an anonymous survey at an urban university in 2001/02. The survey included demographic items and various standardized psychological and health behavior measures. The item "Do you drink caffeinated coffee on a daily basis?" (Y/N) was used to categorize women as Daily (N=19; DC) or Non-daily (N=97; NDC) coffee drinkers. PMS symptoms and their severity were measured by the Shortened Premenstrual Assessment Form (Allen et al., 1998). T-tests and chi-square analyses were used to compare symptoms and symptom severity.
Results: DC women had higher PMS severity scores than the NDC women for 13 of the 20 PMS symptoms ($.002 < p < .05$). Differences were most prominent in the affective domain (e.g., feel anxious, unable to cope, sad/blue). The 2 groups differed in the number of somatic domain symptoms as well (e.g., bloating, edema, skin problems).
Conclusions: DC college women reported higher PMS symptom severity than NDC women, suggesting greater risk for adverse medical and psychological problems. While this study was completed before energy drinks gained popularity (Obrien et al., 2008), findings bolster the need for more research to determine if similar patterns are present in a contemporary cohort of college women.
Financial Support: This research was supported by the Institute for Women's Health and the CTSA at Virginia Commonwealth University.

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ERK AND CREB ARE ASSOCIATED WITH COCAINE-INDUCED CONDITIONED PLACE PREFERENCE.

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Aims: The development and maintenance of cocaine addiction and relapse after abstinence have been shown to depend heavily on learned associations between environmental stimuli and the rewarding properties of the drug. However, not much is known about gender differences in the molecular mechanisms that lead to the formation of these environmentally cued drug associations. The conditioned place preference (CPP) paradigm exploits the neural circuitry underlying the reward, learning, and memory processes of the brain, allowing us to explore the maladaptive neural and molecular changes that occur during the formation of these associations. The present study aimed to investigate the potential gender differences in the molecular mechanisms underlying cocaine-induced CPP in male and female rats.
Methods: Male and Female Fischer rats were conditioned with one of two doses of cocaine (5mg/kg, i.p. or 20mg/kg, i.p.), using a standard CPP procedure.Rats were tested for a preference for the cocaine-paired environment in a drug-free state 24 hours after the last conditioning session.
Results: We found that CPP behavior was expressed in both male and females only in response to the higher dose of cocaine and that this was associated with an increase in p-ERK levels in the nucleus accumbens in males and p-CREB levels in the hippocampus in males upon re-exposure to the cocaine-paired environment.
Conclusions: This study provides evidence for the role of the ERK and CREB signaling pathways and gender differences in the expression of cocaine-induced CPP and retrieval of cocaine-associated memories.
Financial Support: This work was supported by DA12136, RR-024996, RR-03037 and PSC-CUNY.

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PREVALENCE OF SUBSTANCE USE: A COMPARISON OF ADULT AMERICAN INDIANS OF THE NORTHERN PLAINS TO THE NATIONAL HOUSEHOLD SURVEY ON DRUG ABUSE.

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Aims: Compare past year substance use rates of AIs to national survey data, examine AI gender differences in alcohol use, and describe the frequency of substances used among AIs.
Methods: National survey data came from the Substance Abuse and Mental Health Services (SAMHSA) National Household Survey on Drug Abuse which included respondents aged 12 and older in 2000 (n = 71,764). AI data came from a larger study of four reservations in the Northern Plains (NP) of the U.S. A total sample of approximately 5,000 AIs aged 16 and older completed a 200-item questionnaire concerning alcohol/drug use, culture, and demographics.
Results: Results showed no significant difference between AIs' use of alcohol, cocaine, crack cocaine, heroin, hallucinogens, and tranquilizers in the past year compared to national data. However, AIs had significantly higher odds of using cigarettes (odds ratio, 3.83, $p < .01$), smokeless tobacco (odds ratio, 2.84, $p < .05$), marijuana (odds ratio, 2.88, $p < .05$), and stimulants (odds ratio, 7.45, $p < .05$) in comparison to national survey respondents. The substance used most frequently in the past year by AIs was alcohol, followed by cigarettes. Among AIs, significant gender differences were found in past year abstention from alcohol, with 42.4% of females versus 29.8% of males reporting no past year alcohol use ($p < .01$).
Conclusions: Overall, results suggest higher AI use rates of certain substances, high abstention rates from many other substances, and significantly higher abstention rates from alcohol among AI females, which represents a potential protective factor. Due to these complex findings, future research is needed that examines the relationship between these high use and abstention rates. When we have a better understanding of substance use prevalence/abstention among AIs, we can identify risk and protective factors and develop culturally appropriate treatment for AIs.
Financial Support: NIAAA RO1 AA9440; NIAAA R01 AA11685; NIAAA U01 AA11685

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FOUR- AND EIGHT-MONTH OUTCOMES FROM A RANDOMIZED PEER-PARTNERED CASE MANAGEMENT INTERVENTION AMONG COMMUNITY-RECRUITED FEMALE OFFENDERS.

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Aims: Females are increasingly represented in the US criminal justice system with two-thirds incarcerated for non-violent offenses, including drug-related charges. Drug use and associated sexual risk behaviors increase the risk for HIV/AIDS. Interventions that target female offenders in the community or in the system are lacking. The present analyses aim to evaluate changes in female offenders crack cocaine use and sex trading 4 and 8 months post a randomized peer-partnered case management intervention (PPCMI).
Methods: The Sisters Teaching Options for Prevention (STOP) project enrolled female offenders from Drug Courts into a community-based HIV intervention aimed at reducing drug use and sexual risk. Female offenders (n=319) were interviewed in private at a community site and randomly assigned to a standard intervention (SI) or PPCMI. Follow-up interviews were conducted at 4 and 8 months; 249 women completed all 3 interviews.
Results: The sample was primarily African-American (72%), never married (64%), undereducated (44% LT HS), and had been arrested, on average, 11.6 times. Drug use was significantly reduced over the study period for women assigned to the PPCMI, from an average of 23.4 crack cocaine uses per month at baseline to 6.7 uses at 4 and 12.1 uses at 8 months. Women assigned to the SI maintained the level of crack cocaine use reported at baseline, with 14.4 uses per month at baseline, 18.8 uses at 4 and 15.4 uses at 8 months. Overall, the mean number of sex partners dropped from 6.5 at baseline to 2.2 at 4 and 1.8 at 8 months. A third of the sample reported sex trading in the four months prior to baseline, but only 15% of those in PPCMI reported sex trading at 4 and 9% at 8 months compared to the SI, where 21% reported sex trading at 4 and 14% at 8 months.
Conclusions: These results indicate that the PPCMI is a promising intervention for reducing drug use and sexual risk behaviors among high-risk, female offenders. Predictors of favorable outcomes will be further explored.
Financial Support: NR009180, PI: Linda B. Cottler

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PREDICTORS OF HIV STATUS AMONG LOW-INCOME MSMW IN THREE CITIES.

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Aims: To examine risk factors and social ties associated with positive HIV status among low-income men who have sex with men and women (MSMW).
Methods: MSM and drug users were recruited through respondent-driven sampling to provide interview data on HIV risk behaviors. From the full sample recruited in Los Angeles, Raleigh-Durham, and Chicago (n=8,355), we selected a subsample of MSMW (n=796). Logistic regression models were fit to the data to test hypotheses about behavioral risk factors and social ties associated with HIV positive status.
Results: In multivariable models, the following factors were associated with higher odds of HIV positive status: more lifetime male than female partners (OR 6.85, 95% CI 3.45 – 13.6); use of methamphetamine in the past six months (OR 3.25, 95% CI 1.39 – 7.55); unprotected receptive anal sex in the past six months (OR 2.42, 95% CI 1.11 – 5.29); and being recruited into the study by a drug-using MSM (OR 6.38, 95% CI 2.77 – 14.70). Use of crack cocaine the past six months was associated with lower odds of HIV positive status (OR .37, 95% CI .19 - .72).
Conclusions: Findings suggest heterogeneity among MSMW with regard to risk factors associated with HIV positive status. The risk of MSMW transmitting HIV from MSM to women may be higher for MSMW with certain risk characteristics and social ties. Findings underscore the need for targeted prevention interventions and for further study of differences in behavioral risks between groups of MSMW.
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ASSESSMENT OF JAPANESE STIMULANT CONTROL LAW OFFENDERS USING THE ADDICTION SEVERITY INDEX-JAPANESE VERSION: COMPARISON WITH PATIENTS IN TREATMENT SETTINGS.

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Aims: Although many Japanese methamphetamine abusers have received only punishment rather than medical treatment, drug-abuse problems in Japanese prisoners (inmates) have not been sufficiently investigated. The present study assessed problems in inmates who abused methamphetamine.
Methods: Fifty-two male inmates were assessed in 2005-2007 using the Addiction Severity Index-Japanese version and compared with 55 male methamphetamine abusers in hospitals and recovery centers.
Results: The chi-square and Mann-Whitney-Wilcoxon tests showed that the inmates had a significantly lower education level, more frequently had full-time jobs, had more experience living with a sexual partner, and more frequently had a history of juvenile delinquency and criminal records than patients. Although psychiatric symptoms, such as depression, anxiety, and hallucinations, were not common among inmates, suicidal behavior and trouble controlling violence were common in both groups.
Conclusions: These findings suggest that Japanese methamphetamine abusers in correctional settings have many characteristics and environmental backgrounds that are different from abusers in medical settings. Methamphetamine abusers in correctional settings may need to have their specific problems assessed, including trouble with mental health and access to support facilities.
Financial Support: Ministry of Education, Culture, Sports, Science and Technology of Japan (government department; 17025054), the Ministry of Health, Labour and Welfare of Japan (government department; H19-Iyaku-023, H17-Pharmaco-001), the Japan Society for the Promotion of Science (quasi-governmental organization; 17730421, 17591238), and the Mitsubishi Foundation for Social Welfare Activities.

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EVIDENCE FOR MOLECULAR CHANGES IN THE CIRCADIAN SYSTEM FOLLOWING MDMA TREATMENT.

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Aims: MDMA is a psychoactive compound which has marked effects on serotonergic neurons. Previous research has demonstrated that serotonergic agents can affect the circadian pacemaker located in the suprachiasmatic nuclei (SCN) of mammals. As studies in rats and hamsters have found changes in both the behavioral activity rhythm and the response to light following MDMA, the aim of the present study was to investigate changes in core clock genes the SCN (Per1, Per2) and c-fos following MDMA administration.
Methods: Male Long–Evans rats were administered MDMA (5mg/kg i.p.) or saline at either ZT6 (2pm) or ZT16 (12am). The rats were killed 30, 60, or 120 min post-treatment and their brains removed and stored in RNAlater®. Both SCN were punched out and mRNA extracted using Ambion RNAqueous® micro kits (Ambion, Texas, USA) and reverse transcribed into cDNA. Using specific primers for c-fos, Per1 and Per2, the cDNA was amplified by Real Time PCR (RT-PCR). Expression of the mRNA of the genes of interest was determined relative to the expression of β-actin mRNA.
Results: Following MDMA administration at ZT16, c-fos mRNA was significantly increased (~2-fold) 30 min post-treatment, and both Per1 and Per2 mRNA were significantly increased by ~1.8 fold at 60 min post treatment, respectively (all $p < .05$). Following MDMA administration at ZT6, c-fos mRNA was significantly increased by ~1.6 fold 120 min post-treatment, but there were no changes in Per1 or Per2 mRNA levels.
Conclusions: A single dose of MDMA induced in a time of day dependent manner, the expression of 2 core clock genes involved in the generation and maintenance of circadian rhythmicity. These results provide compelling evidence that the sleep complaints reported by ecstasy users may at least in part be mediated by disturbance of the circadian regulation of sleep-wakefulness.
Financial Support: This project received no external funding support.

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EFFECTS OF TIZANIDINE AND NIFEDIPINE IN METHADONE-MAINTAINED HUMANS UNDER A NALOXONE NOVEL-RESPONSE DISCRIMINATION PROCEDURE.

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Aims: Previously, we showed that the alpha2-adrenergic agonist clonidine partially and the dihydropyridine L-type calcium channel blocker isradipine fully attenuated the discriminative stimulus effects of naloxone (NX). The present study examined whether these findings extend to other agents in the same respective classes. Thus, the efficacy of the alpha2-adrenergic agonist tizanidine (TZN) as well as the dihydropyridine L-type calcium channel blocker nifedipine (NFP) to attenuate the behavioral effects of NX was examined 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 TZN (0, 4, 8 12 mg) and NFP (0, 10, 20 mg) each alone and in combination with the training dose of NX were tested.
Results: Thus far, 3 participants have completed the TZN-NX dose sequence and 2 participants completed the NFP-NX test dose. TZN alone produced predominantly placebo-appropriate responding, except that it produced approximately 20% NX- and novel-appropriate responding, respectively, at the 12 mg dose. When administered with NX, TZN produced 100% NX-appropriate responding at all doses. NFP alone produced only placebo-appropriate responding. When administered with NX, NFP produced 100% NX-appropriate responding at all doses tested.
Conclusions: These very preliminary results suggest that, unlike other similar agents examined in this paradigm, neither TZN nor NFP attenuate the discriminative stimulus effects of NX.
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NEIGHBORHOOD CORRELATES OF ILLICIT CIGARETTE SALES IN NYC.

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Aims: New York City (NYC) has among the highest cigarette taxes in the nation with a combined NYC and NY State tax of $4.25 per pack. Previous focus group research has documented an underground tobacco economy. Here we describe neighborhood compositional factors associated with illicit cigarette sales.
Methods: From 2008-2009 we conducted biannual evaluations of the physical and social features of 55 NYC neighborhoods, including the presence of illicit cigarette sales. We combined these observations with neighborhood compositional data on race/ethnicity, income, poverty, unemployment, age, and education from the 2000 U.S. Census. We used t tests to compare neighborhood compositional factors between neighborhoods with and without illicit cigarette sales.
Results: Of the 55 neighborhoods evaluated, 4 (7.3%) were observed to have illicit cigarette sales. Neighborhoods with illicit cigarette sales had a significantly higher proportion of residents living below 200% of the U.S. poverty level (69.3% vs. 55.4%, $p<0.001$) and a significantly lower proportion of White (1.9% vs. 16.6%, $p<0.001$) and Asian/Pacific Islander residents (0.4% vs. 6.1%, $p<0.001$). Neighborhoods with illicit cigarette sales had a marginally higher proportion of Hispanic residents (58.5% vs. 36.1%, $p=0.097$) and residents with less than a high school diploma (53.3% vs. 39.3%, $p=0.098$). We did not observe significant relationships between illicit cigarette sales and unemployment, proportion of black residents, proportion of residents aged 18-24, or proportion of residents aged ≥ 65.
Conclusions: In addition to high cigarette taxes NYC has mandated smoke-free work places, increased education, and distributed free nicotine patches; an 11% decrease in the number of adult smokers was reported for 2002-2003. These findings suggest that anti-smoking programs may be undermined by illicit cigarette sales in disadvantaged and minority neighborhoods.
Financial Support: This study was funded by NIDA (5R21DA025343-02).

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A RANDOMIZED CLINICAL TRIAL OF A COMPUTER-DELIVERED BRIEF INTERVENTION FOR POST-PARTUM DRUG, ALCOHOL, AND TOBACCO USE: THREE-MONTH OUTCOMES.

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Aims: Technology may facilitate implementation of primary-care based screening and brief intervention (SBI). The Motivation Enhancement System (MES) is a single-session, computerized SBI system for use with post-partum women. Pilot data has supported the efficacy of the MES for drug use, but replication and extension to include alcohol and tobacco use are necessary.
Methods: Post-partum women (N = 350) reporting substance use prior to pregnancy were randomly assigned to the MES plus a tailored handout, or to a time control condition. The present analysis focuses on three-month outcomes.
Results: Participants in this study were predominantly African-American (85.8%) and low SES. Although polysubstance use was common, the MES used an algorithm to sort participants into single-focus intervention groups: illicit drug use (n = 143); problem alcohol use (n = 123); and tobacco use (n = 84). At three-month follow-up, advantages for participants receiving the brief intervention were apparent for drug use (58.5% in the MES condition had any past 3-month use, vs. 84.3% of controls; OR = 3.8, p = .004), but not for tobacco (89% in both conditions were cotinine-positive at 3-month follow-up, ns) or alcohol (10.3% in the MES condition were binge drinking monthly or more, vs. 22.2% for controls; OR = 2.5, p = .23). Notably, alcohol use was low in the alcohol subgroup: mean drinks/week at follow-up was 3.7 for the MES condition and 4.7 for controls (Mann-Whitney U = 609.5, p = .32).
Conclusions: Results support earlier findings of MES efficacy in reducing drug use. Positive effects for alcohol were less apparent, with effects in the expected direction but NS, perhaps in part due to low levels of drinking in this subgroup. In contrast, post-partum tobacco use proved resistant to change, with 9 out of 10 women in both groups continuing to smoke. Findings support use of the MES to target post-partum drug use.
Financial Support: Supported by NIDA, R01 DA021329 (Ondersma)

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ASSOCIATIONS BETWEEN AMPHETAMINE-INDUCED DOPAMINE RELEASE AND REAL-TIME IMPULSIVE RESPONDING.

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Aims: There is increasing evidence that impulsivity is a multidimensional construct and that different dimensions and associated risks for drug abuse may be mediated by different neural pathways. The purpose of this study was to examine these relationships.
Methods: Sixteen healthy adults (M=11) ages 18 – 29 years underwent two consecutive 90-minute PET studies with [11C]raclopride (RAC). The first scan was preceded by intravenous saline; the second by 0.3 mg/kg amphetamine (AMPH). Dopamine release (DAR) was defined as percent change in RAC binding potential (BP) between scans in the left (LVS) and right (RVS) ventral striatum. Subjects also completed a set of behavioral performance tasks that assessed risk-taking, response inhibition, tolerance for delayed reward, and premature responding. Self-report measures of sensation-seeking, impulsivity, and stress were also obtained.
Results: Lower tolerance for delayed reward was associated with higher RVS DAR ($p=.035$), as well as higher baseline BP ($p=.035$). A positive relationship was also observed between risk-taking and RVS DAR ($p=.093$). However, a significant interaction was noted with stress on this measure ($p=.082$). High risk takers had greater DAR than low risk takers if they reported low life stress. The reverse was true for subjects under high stress. Greater impulsivity on any of the behavioral measures, except risk-taking, was associated with more pleasant subjective drug effects. No associations were found between self-report measures of impulsivity and DAR. However, greater sensation-seeking was associated with more pleasant drug effects; a negative relationship was found between boredom and LVS BP.
Conclusions: Findings suggest that behavioral measures may be more useful than self-report measures for studying mechanisms that underlie relationships between impulsivity and risks for drug abuse. VS DA responses to AMPH seem to be more closely linked to reward sensitivity and risk-taking traits than to response inhibition.
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NALTREXONE+BEHAVIORAL INTERVENTION COMPARED TO USUAL CARE: DRUG USE AND HIV RISK OUTCOMES IN MEN WITH DRUG-FREE FEMALE PARTNERS.

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Aims: Conducted in the Republic of Georgia, this project tested a novel treatment intervention aimed at engaging, retaining, and treating opioid-dependent men who had drug-free female partners.
Methods: 40 opioid-injecting men and their drug-free female partners were randomized to either an enhanced intervention or a usual care condition. The enhanced condition, Naltrexone+behavioral Intervention (N+BI), consisted of three elements: (1) medication treatment (detoxification followed by naltrexone) for the male partner; (2)
modified versions of both Motivational Interviewing/Motivational Enhancement Therapy (MI/MET) provided to both the male partner and the couple (including HIV/AIDS education); and (3) drug-abstinence incentives in the form of monetary-valued vouchers. The usual care (UC) condition consisted of once a week individualized education sessions. Treatment took place over a 22-week period in both conditions.
Results: Compared to the UC condition, the N+BI condition had significantly more urine samples negative for illicit opioids during the 22-week treatment phase (7.0 v. 1.4, $p < .001$). At 6-month follow-up, the N+BI condition reported significantly less injection of illicit drugs than did the UC condition (17% v. 73%, $p=.012$), and significantly less needle- and syringe-sharing than did the UC condition (0% v. 45%, $p=.014$).
Conclusions: Among opioid-dependent adult males, Naltrexone treatment combined with tailored behavioral therapy and contingency management proved superior to usual care, as it resulted in less opioid use during the course of treatment, and less injection of illicit drugs and a virtual absence of injecting–drug-risk behavior at 6-month follow-up.
Financial Support: The study was supported by international supplement to NIDA grant R01DA13496-03A1 (Hendrée E. Jones, PI)

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OBSERVED THERAPIST BEHAVIORS AND THEIR EFFECTS ON ADOLESCENT AND FAMILY OUTCOMES IN FUNCTIONAL FAMILY THERAPY FOR ADOLESCENT SUBSTANCE ABUSE.

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Aims: To evaluate the Functional Family Therapy Coding and Rating Scale (FFT CARS) which is an observational measurement instrument for classifying discrete moment-by-moment therapist behaviors during sessions of Functional Family Therapy for adolescent substance abuse.
Methods: Two novice graduate level research assistants were trained to use the FFT CARS. A pilot sample of 63 digitized video recorded sessions of FFT was selected at random for the study. The coders viewed each FFT session using a sophisticated digital video data acquisition and management system. Digital mpeg files were viewed and coded "on the fly" using a numerical key pad connected to a Windows-based computer coding terminal.
Results: Ten of the 63 sessions were cross coded to assess inter-rater agreement. Agreement between coders was indexed according to Cohen's kappa. We obtained a kappa coefficient of .60 which is in the moderate to substantial range. Next, specific variables from the FFT CARS were incoporated into a process-outcome analysis of the link between therapist behaviors and adolescent and family outcomes. Using a longitudinal stuctural equation modeling analytic approach, we found that increases in levels of mother-reported family functioning from pre- to post-treatment were predicted by therapists' use of family-focused meaning change interventions as well as individually focused interventions. Increases in mother-reported family functioning, in turn, predicted decreases in adolecent-reported delinquent behavior.
Conclusions: This study is one of the first to establish empirical linkages between therapist in-session behaviors, targeted changes in family functioning, and adolescent behavioral outcomes in family therapy. The results of the study provide strong support for the FFT CARS as a bona fide instrument for capturing theory-based therapist behaviors and clinical processes during sessions of FFT.
Financial Support: This study was funded by a grant from the National Institute on Drug Abuse (R03DA021221).

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IDENTIFICATION OF VOLATILE COMPONENTS IN SMOKELESS TOBACCO PRODUCTS USING HEADSPACE SOLID PHASE MICROEXTRACTION AND GAS CHROMATOGRAPHY/MASS SPECTROMETRY.

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Aims: To identify nicotine and flavor compounds used to enhance consumer appeal of novel smokeless tobacco products using a SPME method.
Methods: Smokeless tobacco products Marlboro Snus, Camel Snus, and Copenhagen moist snuff were analyzed using a HS-SPME-GC/MS method. A CAR/PDMS fiber was used for the extraction of volatile components from the samples. The components were separated by gas chromatography using a DB-5MS capillary column. The oven temperature program was set to 40°C (1 min), and then ramped at 5°C/min to 250°C. The MSD heater transfer line was at 250°C. Temperatures of the quadrupole and ion source were 150 and 230°C, respectively. Analytes were detected after electron impact ionization in SCAN-mode from m/z=50-300. An internal standard was used to calculate relative response factors. Identified compounds were categorized based on chemosensory characteristics and/or their influence on use behavior.
Results: Volatile components including nicotine, menthol and tetramethylpyrazine were identified. The relative amounts of the volatile components are attributed to variation in product sub-brands, as well as to specific analytical parameters used for testing such as type of SPME fiber used, and interactions of specific compounds or specific mixtures of compounds present with the fiber used. Camel Snus Frost was found to have relatively higher menthol whereas Camel Snus Mellow was found to have significantly lower menthol but higher tetramethylpyrazine. Menthol is used to provide a cooling sensation which masks harsh sensory effects. Tetramethylpyrazine imparts a nutty flavor which is an expected characteristic of the Mellow product.
Conclusions: Nicotine level and flavor additives may be manipulated in these products to create variation in nicotine reward and other chemosensory perceptions, and thus optimize appeal among subgroups of potential users.
Financial Support: National Cancer Institute grant # RO1CA125224

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A 12-WEEK CONTINGENCY MANAGEMENT INTERVENTION TO PROMOTE SMOKING CESSATION IN OPIOID-MAINTAINED INDIVIDUALS.

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Aims: While opioid maintenance is an efficacious treatment for opioid dependence, approximately 84-94% of the population concurrently smokes cigarettes. Despite the high rates of smoking and interest in cessation, little progress has been made in developing an efficacious smoking cessation intervention for this population. We have an ongoing NIDA-funded 12-week trial aimed at examining the efficacy of an intensive contingency management (CM) intervention for opioid-maintained individuals. A prior study by our group showed that an intensive but brief 2-week intervention could produce initial smoking abstinence in this group.
Methods: During the first 2-weeks of the study participants attend the clinic daily and can earn voucher-based reinforcement each time they meet our rigorous biochemical criteria. Vouchers are provided on an escalating schedule that includes a reset for positive samples and bonuses to encourage early abstinence. Following the first 2-weeks, participants are randomized to either an extended contingent (receiving vouchers contingent upon meeting our abstinence criterion) or extended noncontingent (receiving vouchers independent of smoking status) experiment group for the remaining 10-weeks.
Results: Thus far, 35 participants have completed the trial (33 years old, 29% male). During the first 2-weeks of the trial, participants appear to be achieving high levels of total abstinence, with 65% of samples meeting the abstinence criterion. After randomization, the extended contingent group appears to be maintaining superior levels of abstinence compared to the extended noncontingent group with 57.5% and 30% of samples meeting the abstinence criterion, respectively, $p < .05$.
Conclusions: Our CM intervention appears to promote high levels of smoking abstinence during the first 2-weeks, and the extended contingent group appears to be maintaining more smoking abstinence during weeks 3-12 than the extended noncontingent group. Data from the ongoing trial (N=100) will be presented and may hold potential for dissemination to clinics throughout the country.
Financial Support: R01 DA019550 & T32 DA007242

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DOPAMINE TRANSMISSION FOLLOWING ACUTE AND CHRONIC "SPEEDBALL" ADMINISTRATION.

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Aims: Cocaine/heroin combinations (speedball) induce synergistic elevations in extracellular dopamine concentrations ($[DA]_e$) in the nucleus accumbens (NAc) and ventral tegmental area (VTA) compared to cocaine or heroin alone. To delineate the potentiating mechanism by which speedball enhances NAc $[DA]_e$, *in vivo* fast-scan cyclic voltammetry was performed to examine DA release and reuptake kinetic parameters in both chronic and acute paradigms of cocaine, heroin and speedball self-administration (SA).
Methods: Male Fisher rats self-administered cocaine, heroin or speedball for 25 days under a multicomponent session prior to *in vivo* microdialysis, and under a fixed infusion session prior to *in vivo* voltammetry. For voltammetry, rats were anesthetized and implanted with stimulating electrode in the VTA and carbon fiber microelectrode in the NAc. Drug-naïve rats were also implanted with catheters and electrodes in the same manner. Following baseline recordings, i.v. drugs were administered and stimulated DA release was monitored in the NAc.
Results: Microdialysis showed that $[DA]_e$ were synergistically elevated in the NAc during speedball SA (800% of baseline) compared with cocaine (400%) and heroin (150%), and also 400% in the VTA by speedball compared with cocaine (200%) and heroin (150%) alone. In contrast, electrically evoked DA was greater following acute cocaine compared to speedball. In chronic SA rats, evoked $[DA]_e$ was similar after cocaine and speedball. DA transporter (DAT) apparent affinity (K_m) was similarly elevated following cocaine and speedball in both paradigms. Futhermore, chronic speedball SA increased baseline maximal DAT uptake rates (V_{max}).
Conclusions: Increased DA clearance was consequence of synergistic NAc $[DA]_e$ elevations by speedball. Although the exact mechanism for these supra-additive effects remains unclear, our findings support current hypotheses for elevated mesolimbic DA cell firing rates due to combined disinhibition by heroin and impaired reuptake by cocaine.
Financial Support: NIH/NIDA R01 DA012498 and DA021534.

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EFFECTS OF METHAMPHETAMINE ABUSE AND SEROTONIN TRANSPORTER GENE VARIANTS ON AGGRESSION AND EMOTION-PROCESSING NEUROCIRCUITRY.

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Aims: Methamphetamine (MA) abuse is associated with heightened aggression. MA abuse itself and genetic variability in the serotonin transporter (SERT) gene may both contribute to this behavior. This study aimed to test whether common SERT risk allele frequencies differ between MA-dependent and healthy control (HC) individuals, and to evaluate effects of MA abuse and genotype on aggression and associated neurocircuitry.
Methods: MA-dependent (N=53) and HC (N=47) human research participants were genotyped at two functional polymorphic loci in the SERT gene (SLC6A4-LPR and intron 2 VNTR) and were classified as high or low risk for aggression according to individual allele combinations. Subsets of participants completed the Aggression Questionnaire (AQ) and functional magnetic resonance imaging while observing emotional faces.
Results: Chi2 analyses found no differences in risk-allele loads between MA and HC groups. ANOVA of AQ scores showed higher aggression in MA than HC, and in high-risk than low-risk participants, but no interaction. Region-of-interest analysis showed lower amygdala signal change in high-risk than low-risk participants, but no effect of MA abuse or interaction. Whole-brain analyses showed differences between MA and HC in occipital and prefrontal cortex (PFC), and between low- and high-risk genetic groups in occipital, fusiform, supramarginal and PFC regions, with overlap in right ventrolateral PFC.
Conclusions: The study found similar SERT risk allele loads between groups, and no interaction between MA abuse and genetic risk. MA and genetic risk may influence aggression independently, with minimal overlap in associated neural substrates; i.e., deficits associated with MA abuse may add to predisposing genetic influences.
Financial Support: R01 DA020726, R01 DA015179, and P20 DA022539 (EDL); F31 DA025422 (DEP); T90 DA022768 and T32 DA024635; M01 RR00865 (UCLA GCRC); and endowments from the Pike Chair in Addiction Studies and the Green Family Trust (EDL).

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THE INFLUENCE OF SOCIAL INTERACTIONS AND NICOTINE ON CORTICOSTERONE AND BEHAVIORAL RESPONSES IN FEMALE AND MALE ADOLESCENT RATS.

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Aims: Adolescence is a critical period for social reward and the initiation of nicotine use; therefore we systematically compared the behavioral and neuroendocrine responses to nicotine in both male and female mid adolescent (P39) Sprague-Dawley rats during isolation or social interactions.
Methods: Locomotor activity and play behaviors were evaluated for 15 min following injections of either saline or nicotine (0.6 mg/kg, s.c.). Immediately following testing, animals were sacrificed and blood samples were collected in order to measure plasma corticosterone levels using ELISA.
Results: Nicotine pretreatment increased plasma corticosterone in both sexes in isolate tested rats, and attenuated several indices of play behavior including nape attacks, pins and social contact; there was no effect of nicotine on locomotor activity in either isolate or social groups. Social interactions prevented the nicotine-induced elevations in corticosterone in both males and females.
Conclusions: These results suggest that the presence of a social partner may decrease the initial negative, stress-activating effects of nicotine. In turn, nicotine rewarding effects would be enhanced.
Financial Support: Supported by DA025413, DA11064, DA023123, F31DA023746 and MGE@MSA.

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GENDER DIFFERENCES AND SIMILARITIES IN SEXUAL RISK BEHAVIOR: IMPLICATIONS FOR ASSESSMENT AND INTERVENTION IN SUBSTANCE ABUSE TREATMENT SETTINGS.

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Aims: While the connection between substance abuse and sexual risk behavior is a robust and reliable one, the nature of this relationship becomes more complex when considering gender differences. Women in substance abuse treatment may engage in more or different types of risk behavior than men, and men's and women's behaviors may be differentially altered by treatment or by HIV prevention efforts. The purpose of this project is to examine gender differences within data from an ongoing pilot study involving integrating sexual risk reduction into substance abuse treatment.
Methods: An audio computer assisted interview (ACASI) sexual risk assessment was administered to 61 men and 48 women seeking outpatient substance abuse treatment. Investigators examined gender differences in sexual risk behavior.
Results: A higher percentage of women reported having a main partner (87.5%) than men (48.3%; $\chi 2 = 18.16$, $p < .001$), a higher proportion of men reported no sexual partners in the past 90 days (50.0%) than women (8.3%; $\chi 2 = 24.25$, $p < .001$), and women endorsed having riskier partners at a higher rate (31.6%) than men (15.4%; $\chi 2 = 2.82$, $p = 0.093$). No gender differences were identified for the following variables: sex under the influence of drugs or alcohol during the last sexual event, condom use during the last sexual event, sex with a casual (versus committed) partner during the last sexual event, sense of self-risk for HIV, and possession of condoms.
Conclusions: Although other literature suggests pronounced gender differences in sexual risk behavior, we found few differences in our sample. Because more women reported being partnered, and that their partners are perceived as riskier, future studies may benefit by including assessment of relationship safety, sexual assault in the context of relationships, and confidence in talking about sexual issues with partners. Furthermore, our results have implications for tailoring interventions for women to include skill building for maintaining healthy relationships.
Financial Support: NIDA grant R21DA022940 (D. Calsyn, PI)

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QUALITY OF LIFE IN CRACK, COCAINE AND OTHER PSYCHOACTIVE SUBSTANCE ABUSERS WHO SEEK TREATMENT IN FOUR BRAZILIAN CAPITALS.

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Aims: Over the past years, Brazil has faced an increase in crack consumption. There are studies showing an important association between substance abuse and lower quality of life, but there is still little information about this association in crack users. The aim of this study was to compare the quality of life among crack users, cocaine snorers and other psychoactive substance abusers in four Brazilian capitals.
Methods: Methods: Cross-sectional study of a convenience sample of 735 drug abusers (293 crack users, 126 inhaled cocaine, and 322 for other drugs – mostly alcohol and marijuana), recruited from hospitals or clinics specialized in treating substance abuse in four Brazilian state capitals. The interviewers were psychologists who were trained and tested for reliability. Quality of life and substance abuse were ascertained by The World Health Organization Quality of Life (WHOQOL-Bref) and The Sixth version of the Addiction Severity Index (ASI6).
Results: Results: Quality of life was significantly poorer with regard to the psychological domain in the crack and cocaine abusers (51.8±20.4) when compared to other substance abusers (57.2±18.9). There were no differences in other areas. Crack users had statistically significant more illegal activities (50±17.1) than other substance abusers (12±3.8).
Conclusions: These findings corroborate previous studies showing an association between crack and cocaine abuse and poor quality of life. On the other hand, it is not clear whether this impairment is associated with the lifestyle of this population, crack use, comorbidity or to the use of different kinds of substances at the same time. Also, this was one of the first studies to use the Addiction Severity Index (ASI6) in the Brazilian population, which made possible to obtain a better panorama of problems faced by drug users.
Financial Support: Secretaria Nacional Antidrogas

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PREDICTORS OF LOST-TO-CARE VS. ENGAGED STATUS AMONG URBAN HIV CLINIC PATIENTS.

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Aims: Aims: Recent advances in HIV pharmacotherapy have enabled HIV+ patients to live longer and with enhanced quality of life, but suboptimal adherence is associated with emergence of resistant viral strains, reduced responsiveness to treatment, and transition to AIDS. This study was conducted to determine if, relative to a comparison group of engaged/medication adherent patients (E), Lost-to-Care (LTC) patients differ in prevalence of substance use, housing status, psychiatric symptoms, dysfunctional treatment interfering beliefs, and hopelessness.
Methods: Methods: A pilot study attempting to distinguish LTC (missing from treatment for more than 6 months) and engaged patients (E; attended more than 75% appointments and medication compliant) was conducted at an urban HIV clinic. A total of 79 subjects (36 LTC; 43 E) completed a battery of psychological tests.
Results: Results: Preliminary analysis was performed using direct logistic regression on treatment status (LTC; E) as outcome and eight predictors: housing stability, illicit drug use within the past 30 days, lifetime months of incarceration, Beck Depression Inventory total score, Beck Hopelessness Scale total score, negative life events, satisfaction with social support, and HIV-related dysfunctional beliefs. A test of the full model with all predictors against the constant-only model was statistically reliable, x2 (8, N=79) = 32.22 (p=. 000), indicating that the predictors, as a set, reliably distinguished between LTC and E. The variance in treatment status accounted for was good, with Nagelkerke R2=.45 and 78% of LTC and 77% of E correctly predicted for an overall rate of 77%. According to the Wald criterion, only stability of housing (x2=8.57, p<. 01), illicit drug use in the past 30 days (x2=4.28, p<. 05), and lifetime months of incarceration (x2=3.98, p<. 05).
Conclusions: Conclusions: These data show that LTC clearly differ from E patients. Particular areas of concern for LTC patients include housing instability and substance use.
Financial Support: Financial Support: NIDA P60 DA005286-21 (O'Brien); U10 DA-13043 and KO5 DA-17009 (Woody)

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PTSD PREDICTS TREATMENT-SEEKING AND DRUG USE IN SYRINGE EXCHANGE PARTICIPANTS.

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Aims: Injection drug users who are not in treatment have very high rates of traumatic event exposure, and over 20% develop posttraumatic stress disorder (PTSD). Traumatic event re-exposure in this population is associated with short-term increases in treatment-seeking and drug use (Peirce et al., 2010). While PTSD is an enduring consequence of traumatic events, few studies have examined relationships between PTSD and proximal outcomes in out-of-treatment drug users. The present study examines the effect of PTSD on treatment-seeking and drug use in a sample of 162 injecting drug users enrolled in syringe exchange.
Methods: Participants were assessed for PTSD using the Modified PTSD Symptom Scale-Revised (MPSS-R; Falsetti et al., 1993) at baseline and months 4, 8, and 12 of the 16-month study. Self-reported treatment-seeking and drug use were assessed every month. The association of PTSD with treatment-seeking and drug use was tested with Generalized Estimating Equations (Zeger & Liang, 1988).
Results: Participants with PTSD were twice as likely to report an interest in substance abuse treatment in the same month [OR (95% CI)=2.08 (1.23-3.52)]; this relationship held for treatment interest the next month [2.54 (1.59-4.05)] and two months after diagnosis [1.74 (1.12-2.72)]. Drug use outcomes were more mixed. PTSD was associated with a greater likelihood of daily heroin use only in the same month [1.79 (1.12-2.87)]. Participants with PTSD were more likely to report cocaine use in the same month [1.57 (1.02-2.43)] and two months later [1.91 (1.16-3.13)].
Conclusions: These results stand in contrast to our previous data showing that traumatic event re-exposure alone intensified both desire for treatment and drug use only for a short time. In contrast to traumatic event re-exposure alone, PTSD appears to precipitate a more long-lasting increase in treatment-seeking and, to a lesser extent, drug use.
Financial Support: This research was supported by K23DA015739 (Peirce) & R01DA012347 (Kidorf).

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THE ISOFLAVONE PUERARIN REDUCES ALCOHOL INTAKE IN HEAVY DRINKERS.

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Aims: Isoflavone compounds naturally occurring in the root of the kudzu plant have been used historically to treat alcohol-related problems. Numerous preclinical studies have shown that these compounds reduce drinking in a number of animal models. A recent study in our laboratory showed that a purified extract of the kudzu root containing three primary isoflavones reduced drinking in humans. The present study assessed the effects of one primary isoflavone – puerarin- for its ability to modify alcohol intake in humans.
Methods: Nine healthy adult volunteers who drank on average 18.1 ± 10.2 drinks per week, completed the study (7 men, 2 women). They were 25.9 ± 3.4 yrs old, Caucasian (1 of Hispanic descent). Capsules containing 600 mg of puerarin (NPI-031G, Natural Pharmacia Inc, Burlington, MA) were taken twice daily for a total dose of 1,200 mg. The puerarin was administered in a double-blind, placebo-controlled, crossover design for one week prior to an afternoon drinking session lasting 1.5 hours. During the drinking session, participants had access to up to six bottles of their preferred brand of beer in addition to juice and water. Drinking behavior was recorded by a custom-built end table that housed a concealed electronic scale connected to a computer in the next room.
Results: Participants consumed on average 3.29 (± 0.7) beers when treated with placebo and 2.28 (±0.6) beers when treated with puerarin. Participants treated with puerarin delayed opening beers by an average of 10 additional minutes (23% increase), took 4 minutes longer to consume beers (18% increase), and took more sips to drink a beer (11.6 vs. 10.4).
Conclusions: These preliminary results from a small sample size are encouraging as this is the first demonstration that a single isoflavone found in the kudzu root can alter alcohol drinking in humans. These results suggest that alcohol consumption patterns are influenced by puerarin administration and this herbal medication may be a useful adjunct in the treatment of excessive alcohol intake.
Financial Support: Supported by NIAAA Grant R44 AA152200 (D.Y.-W Lee)

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ISSUES FACED BY FEMALE INJECTION DRUG USERS: A REVIEW OF THE LITERATURE.

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Aims: 1) This review will elucidate and explain unique risks and issues faced by female injection drug users in the United States including
a) Gender-specific oppression (poverty, minority status,and stigma)
b) Gendered violence including structural, symbolic, and interpersonal
c) Higher rates of incarceration
d) Increasing rates of Hepatitis C and HIV
e) Higher rates of comorbid mental health issues and trauma
f) Unique injecting practices that put FIDUs at greater risk for infection
2) This review will also demonstrate a need for harm reduction services and policies that have not been widely embraced in the United States (i.e., needle exchange, supervised injection facilities, and methadone maintenance) with a focus on the need for the incorporation of gender-specific services within these existing services.
3) This review will conclude with implications for future research in social work/counseling with regard to female injection drug users including
a) The need for research that aims to understand women's unique injecting experiences.
b) The need for gender-specific interventions that will lower the rates of gendered violence experienced by female injection drug users and address trauma experienced them.
Methods: This review includes research that uses a variety of methods including: semi-structured qualitative interviews based in grounded theory, randomized control trails, quasi-experimental designs, and longitudinal studies.
Conclusions: Female injection drug users are at higher risk for HIV and other blood-borne illnesses due to injection practices and sexual behavior. FIDUs face challenges and health burdens that their male counterparts typically do not face, i.e., sexual violence, childcare issues, and greater risk for HIV.
More knowledge of women's experiences with injecting, different forms of counseling, and different handling of women's issues among practitioners is needed to reduce the unique risks experienced by women who inject. Further studies should be undertaken to address this.
Financial Support: N/A

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IMPULSIVENESS OF TOBACCO AND STREET DRUG ADDICTION: DELAY DISCOUNTING AMONG COMMUNITY CORRECTIONS PARTICIPANTS WHO ARE DEPENDENT ON LEGAL AND ILLICIT SUBSTANCES.

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Aims: Discounting of delayed monetary rewards is a common behavioral phenomenon seen among drug users and criminal offenders. These groups tend to indulge in immediate gratifications despite the negative consequences that might ensue. The purpose of this study is to examine if the presence of substance use disorders add to the impulsive behavior of a population who is already highly impulsive.
Methods: One hundred people were examined who were under community correction supervision and voluntarily participated in a smoking cessation clinical trial. A hypothetical monetary delay discounting measure was administered prior to receiving smoking intervention and all participants were smoking at least 5 cigarettes per day at the time of the assessment.
Results: An independent-samples t test revealed that participants who were dependent on illicit drugs (i.e., within the past 12 months) significantly differed on the discounting task from those who were not dependent on such substances. No specific drug accounted for the difference. Those who only abused drugs did not differ from participants without a substance use diagnosis. In addition, the inclusion of alcohol abuse or dependence in the analysis only confounded the group difference, consequently making the statistical distinction between the groups insignificant.
Conclusions: The findings suggests that smokers who are dependent on illicit drugs are even more impulsive than other smokers - that is, they indulge in immediate gratifications more than smokers without a substance use diagnosis. While cigarette smokers and criminal offenders are groups that are already characterized by impulsive behaviors, substance dependence appears to have an additive effect on these groups: it either exacerbates impulsive nature or those who are excessively impulsive may have a propensity to become dependent on illicit drugs in addition to smoking tobacco and engaging in criminal activities.
Financial Support: This study was supported by UAB Psychiatry Departmental Funds.

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MDMA (ECSTASY) IMPAIRS SHORT-TERM MEMORY RECOGNITION IN RATS.

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Aims: Human and animal studies have demonstrated short-term (or working) memory impairments resulting from the use and/or former abuse of 3,4-methylenedioxymethamphetamine (MDMA), the psychoactive component in ecstasy. However, the mechanism by which MDMA disrupts short-term memory is unknown. The aim of this study was to determine the effect that MDMA has on short-term memory in rats and the mechanism by which MDMA produces those behavioral effects.
Methods: Male Sprague Dawley rats (~300 g) were treated with an established serotonergic neurotoxic regimen of MDMA (IP injection of 0 or 5 mg/kg MDMA, once every 2 hours for a total of 4 injections). Rats were tested for short-term memory recognition using the novel object recognition (NOR) test 2 and 7 days post-administration.
Results: The results show that control rats learn the NOR paradigm and display normal short-term memory recognition at both the 2 and 7 day periods. MDMA administration partially disrupts memory recognition 2 days after drug administration and significantly disrupts memory recognition 7 days afterwards, an effect that was significantly different from control rats.
Conclusions: These data illustrate that a neurotoxic regimen of MDMA administration produces time-dependent, long-lasting effects on short-term memory in rats. Analysis of brain tissue is in progress to determine the neuroanatomical localization and the extent of serotonergic neuronal loss and microglial activation to characterize further the mechanism by which MDMA disrupts short-term memory.
Financial Support: This study was supported by grants from the National Institute on Drug Abuse to Shane Perrine (DA024760) and to David Thomas (DA020680) and a VA Merit award to David Thomas.

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INFLUENCE OF ESTROGEN ON MORPHINE REWARD.

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Aims: Previous research indicates that female rats are more sensitive to the rewarding properties of opiates than male rats. To date, few studies have directly examined the effects of gonadal hormones on the rewarding properties of morphine. The aim of the present study was to investigate the effects of estradiol on expression of conditioned place preference (CPP) to morphine in ovariectomized (OVX) rats.
Methods: Adult female Long Evans rats were OVX and lavaged daily for 10 consecutive days (beginning one week after surgery) to confirm cessation of cycling prior to beginning CPP. Thirty minutes prior to each day of conditioning or testing, rats received a subcutaneous (s.c) injection of 5μg 17β-Estradiol 3 benzoate in 0.1mL of peanut oil (EB) or peanut oil (PO). All CPP experiments were performed during the dark phase of the rats' light/dark cycle using a commercial three chambered CPP apparatus. On Day 1 of CPP, all rats underwent a preconditioning test during which they were allowed to explore the entire apparatus for one 30-minute session. Rats were then assigned to saline/morphine conditioning chambers using a counterbalanced method for a total of six conditioning sessions. On each of the three saline conditioning days, animals received a 1ml/kg s.c. injection of 0.9% saline and were confined to the saline-paired chamber for 1 hour. For each of the three morphine conditioning days, animals received a s.c. injection of morphine sulfate at a volume of 1ml/kg dissolved in 0.9% saline and were placed in the drug-paired chamber for 1 hour. On the day of the Acquisition Test, rats were allowed free access to all chambers for 30 minutes.
Results: Both EB and PO treated OVX rats acquired CPP to 10mg/kg morphine ($p<0.05$). However, acute treatment with EB significantly attenuated CPP in OVX females conditioned with 10mg/kg morphine compared to OVX females treated with PO ($p<0.05$).
Conclusions: These results suggest a role for estradiol in morphine reward in females. Experiments are currently underway to examine a wider range of morphine doses as well as some of the molecular mechanisms underlying these behavioral differences.
Financial Support: Supported by a NARSAD award to LIP.

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SEX DIFFERENCES IN DRUG ABUSE.

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Aims: Drug addiction, specifically cocaine addiction, differentially affects men and women. Compared to men, women increase their consumption of cocaine more quickly and are more sensitive to cocaine's effects. Given these differences and many others, the aim of numerous animal studies has been to analyze biological factors to explain why men and women respond so differently to drugs of abuse, especially cocaine.
Methods: Gonadal hormones, particularly estrogen, play an important role in cocaine addiction. For example, estrogen enhances such cocaine-induced behaviors as locomotor activity (LMA) and conditioned place preference in female rats. Additionally, estrogen has a stimulatory effect on dopamine (DA), whose reuptake is inhibited by cocaine. Becker revealed that estrogen increases dopamine release in the striatum, while Zhang et al. demonstrated that estrogen influences the increased sensitivity of DA neurons to cocaine.
Despite this link between estrogen and dopamine, Becker asserted that estrogen does not solely explain females' increased cocaine sensitivity compared to males. Cocaine-amphetamine regulated transcript (CART) is a peptide that is densely localized in the nucleus accumbens (NAc), a brain region associated with drug reward and reinforcement. CART peptide injection into the NAc inhibits cocaine-induced LMA, possibly through counteracting increased synaptic DA levels after cocaine administration. Interestingly, CART peptide is itself partially regulated by estrogen. Shieh et al. demonstrated CART peptide's dependence on estrogen to increase mesolimbic and nigrostriatal DA turnover. The exact mechanism behind this relationship is not known, but it is proposed that estrogen's intracellular receptors play a stimulatory role. Further study is warranted in this area.
Conclusions: In conclusion, there is a complex relationship between cocaine, estrogen, dopamine, and CART peptide. Further elucidation of each component's influence on the sex differences in drug addiction is critical in not only fully understanding this relationship, but also developing effective and long-lasting treatment for drug addiction.
Financial Support: Supported by NIH grant 5T32DA015040-08.

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TOWARDS DEFINING PRIMARY OUTCOMES IN TREATMENT STUDIES FOR CANNABIS USE DISORDERS: RESULTS FROM CONFIRMATORY FACTOR ANALYSIS OF OUTCOMES FROM THREE RANDOMIZED CONTROLLED TRIALS.

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Aims: While several randomized controlled trials evaluating a range of treatments for cannabis use disorders have appeared in recent years, these have been marked by a relative lack of consistency regarding primary outcome measures, making it difficult to compare outcomes across studies.
Methods: With the aim of identifying salient and reliable indicators of key outcome domains for treatment studies of cannabis use disorders, confirmatory factor analyses were conducted using data from 3 independent randomized controlled trials of behavioral treatments for cannabis use disorders (Carroll et al., 2006; Carroll et al., in preparation; Marijuana Treatment Project Research Group, 2004). To assess the incremental fit of the models of marijuana outcomes, a model with all outcomes as indicators of 3 independent constructs of frequency of marijuana use (e.g., % days of marijuana abstinence during treatment), severity of marijuana use (e.g., Addiction Severity Index [ASI] Drug Composite scores), and psychological distress (e.g., Beck Depression Inventory scores) was compared to an alternative model with all outcomes as indicators of 1 construct.
Results: The best-fitting model of outcomes in each study encompassed 3 factors: frequency of marijuana use, severity of marijuana use, and psychological distress ($p < .01$). Outcomes related to the maximum duration of marijuana abstinence loaded strongly on the factor of frequency of marijuana use, ASI Drug Composite scores loaded strongly on the factor of severity of marijuana use, and depression scores loaded strongly on the factor of psychological distress.
Conclusions: Results can guide future marijuana treatment studies in the collection of relevant outcomes and encourage consistency in the reporting of outcomes across studies. They can also facilitate meta-analyses and comparative outcome studies of treatments for cannabis use disorders.
Financial Support: NIDA T32-DA007238 (ENP, KMC)& P50-DA09241 (KMC,CN)

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ECOLOGICAL MOMENTARY ASSESSMENT OF SELF-IDENTIFIED REASONS FOR SPECIFIC INSTANCES OF DRUG USE AMONG PARTICIPANTS WITH AND WITHOUT HEPATITIS C.

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Aims: Ecological Momentary Assessment (EMA) has been shown to be an effective tool for real-time in the field assessment of behavior. In this analysis, we examined the reasons given for specific instances of drug use, at the moment of drug use, in participants with and without hepatitis C (HCV).
Methods: In a cohort design, a volunteer sample of 112 methadone-maintained cocaine- and heroin-abusing outpatients provided up to 25 weeks of ecological momentary assessment (EMA) data on handheld computers. Participants initiated an entry each time they used cocaine or heroin, and each such entry included yes/no responses to 13 questions beginning, "I think it happened because..." (with response options based on a published taxonomy of relapse triggers). Responses to those questions were compared in individuals with and without HCV using Stata Generalized Estimating Equations for binary outcomes.
Results: Participants with HCV, compared to those without, were more likely to report drug use as a result of feeling bored ($z=2.09$, $p=0.036$), frustrated ($z=2.12$, $p=0.034$), worried ($z=2.53$, $p=0.012$), sad ($z=2.24$, $p=0.025$), or feeling that others had been critical of them ($z=2.21$, $p=0.027$). HCV status was not associated with differences in drug use attributed to handling cash, being in a good mood, feeling uncomfortable, feeling tempted out of the blue, or several other response options.
Conclusions: Participants with HCV were more likely to attribute their specific episodes of drug use to negative moods. The detailed EMA mood and drug use data reported here should help inform treatment interventions aimed at changing environmental triggers.
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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SKIN AND NEEDLE HYGIENE INTERVENTION FOR INJECTION DRUG USERS: PRELIMINARY RESULTS FROM A RANDOMIZED CONTROLLED STAGE I PILOT TRIAL.

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Aims: A new intervention to reduce high-risk practices associated with bacterial (e.g., skin abscesses) and viral (e.g., HIV) infections among injection drug users (IDUs) was developed using a stage model of behavioral therapy, qualitative data from focus groups, past research, and the Information-Motivation-Behavioral Skills Model. The efficacy of the intervention was examined in a randomized controlled pilot trial.
Methods: Active heroin injectors ($n = 48$) were recruited through street outreach in Denver and randomized to either the two-session, skill-based, "Skin and Needle Hygiene Intervention" delivered individually, or an assessment-only control group. Preliminary one-month follow-up data was examined to determine the effect of the intervention on injection practices.
Results: The sample was 75% male, 54% Caucasian, and averaged 43 years of age. One-third of participants were homeless. No between group differences were found at baseline for any of the outcome variables. At the one-month follow-up, drug use and injection frequency decreased more days among those randomized to the intervention than among controls (ns). Those randomized to the intervention had larger reductions on a bacterial infections risk index [$t(45) = 1.92$, $p = .061$, $d = .56$] and on the HIV Risk Assessment Battery ($t(45) = 2.68$, $p = .010$, $d = .78$). Intervention participants also had greater improvements in skin [$t(45) = 8.15$, $p = .000$, $d = 3.64$] and needle cleaning [$t(44) = 12.47$, $p = .000$, $d = 2.40$] behavioral skills, as measured by a videotaped behavioral skills assessment. Seven (29.25%) control participants and only one (4.4%) intervention participant reported an abscess between baseline and the one-month follow-up (Fisher's exact $p = .048$).
Conclusions: The new intervention appears very promising as a brief intervention to reduce risks associated with IDU. Completion of 6-month follow-up data will be examined to determine whether effects are maintained.
Financial Support: Supported by: NIDA 1 R21 DA026773

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DOSE PREFERENCE AND DOSE ESCALATION OF HEROIN IN EXTENDED-ACCESS SELF-ADMINISTRATION IN FISCHER AND LEWIS RATS.

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Aims: Rats that self-administer drugs of abuse over extended periods of time show a characteristic increase of number of infusions over time, until they reach a plateau. Usually, short (1-3 hrs) and prolonged (6-18 hrs) intravenous self-administration (SA) sessions in rats are carried out with a constant unit dose of heroin throughout the experiment. Heroin users will escalate the dose when unlimited amounts of heroin are available. Recently, we published a new self-administration paradigm whereby rats have the possibility to choose between different doses of cocaine, thus escalating the dose as well as the number of infusions. Using this paradigm, our aim was to compare heroin self-administration of two rat strains, Fischer and Lewis, which have a lower and higher sensitivity to the rewarding effects of heroin, respectively.
Methods: Rats were trained to self-administer heroin (50 μg/kg/injection) in two-hour daily sessions. The criteria for the acquisition of SA were reached after 14 days on average. Dose escalation: rats were exposed to extended (18h) self-administration sessions for 14 days. Rats had access to two active levers associated to two doses of heroin. If a rat preferred the lever associated with the higher dose for two consecutive days, then the available doses were raised. During the escalation, four heroin doses were used ranging between 20 to 250 μg/kg/infusion.
Results: After 14 days of exposure to extended self-administration sessions, Lewis rats escalated the total amount of heroin taken per day with almost 50% of rats preferring the 125 μg/kg/infusion dose. Fischer rats, however, never escalated the unit dose and, in general, self-administered very low quantities of heroin. On average, Lewis rats took 52±5.3 μg/kg of heroin daily, whereas Fischer rats took 12.7±0.5 μg/kg.
Conclusions: Our work shows that when different doses of heroin are available, Fischer rats self-administer very low amounts of the drug. On the other hand, Lewis rats escalate the unit dose and the total amount of heroin.
Financial Support: This work was supported by a NIH-NIDA P60-DA05130 grant.

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HIV-1 GP120 INDUCES THE EXPRESSION OF THE TRANSCRIPTION FACTOR NF-E2- RELATED FACTOR 2 IN ASTROCYTES.

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Aims: HIV infection is known to affect the central nervous system resulting in HIV associated neurocognitive disorder (HAND), which is characterized by depression, behavioral and motor dysfunctions. The viral envelope protein gp120 is known to induce the release of neurotoxic factors which lead to apoptotic cell death. Although the exact mechanisms involved in gp120-induced neurotoxicity are not completely understood, studies have shown that oxidative stress plays a vital role in the neuropathogenesis of HAND. Increased oxidative stress is known to induce NF-E2- related factor 2, (Nrf2), a basic leucine zipper transcription factor that is known to regulate the antioxidant defensive mechanism. However, the role of Nrf2 in gp120 mediated neurotoxicity has not been elucidated. We hypothesize that the Nrf2 stimulation may be associated with the activity to preserve the intracellular homeostatic redox status.
Methods: RNA isolated from control and HIV gp120 treated astrocytes were reverse transcribed and analyzed by qRTPCR in order to determine the gene expression levels. Total cell lysates were prepared and analyzed by western blots to examine their protein expression levels.
Results: We report that gp120 significantly upregulates the expression of gene and protein levels of Nrf2 in human astrocytes. In addition, pretreatment of the astrocytes with antioxidants or BAPTA, a calcium chelator significantly attenuated the upregulation of Nrf2.
Conclusions: our results suggest that the astrocytes upregulate their antioxidant defense mechanisms in response to the gp120 induced stress and the consequent elevation of intracellular calcium levels. However the amount of upregulation or the duration of upregulation may not be sufficient to completely protect the cell.
Financial Support: This work was in part supported by RO1DA012366, RO1DA021537,R37DA025576

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SOCIAL EXCLUSION AND ENGAGEMENT IN RISKY SEXUAL BEHAVIOR AMONG FEMALE CRACK COCAINE USERS.

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Aims: Crack cocaine and engagement in sex exchange for drugs represent important contributors to the escalation of the HIV infection among women justfying the need to understand the factors that may increase women's vulnerability for such practices. We suggest that female gender role which emphasizes equality, communion and intimacy may play an important role. Specifically, the experience of social rejection may increase women's perception of self-discrepancy from the socially dictated norms and may be associated with higher rates of deviant behavior such as risky sexual behavior. The present research attempts to examine this hypothesis.
Methods: Crack cocaine using participants reported on the frequency of their engagement in risky sexual behaviors (including sex exchange for drugs) during the past year. Subsequently, they participated in a Cyberball computer game designed to induce the experience of social rejection followed by a self-report questionnaire assessing the level of rejection experienced.
Results: Higher rates of experienced social rejection significantly predicted frequency of engagement in sex exchange, but only among women. Among men, experiencing social rejection during the computer game was not significantly related to their engagement in sex exchange in the context of drug use.
Conclusions: The results of this study indicate that increased sensitivity to rejection following social exclusion is significantly related to engagement in risky sexual behavior among female crack cocaine users. Although preliminary, this finding suggest the need to address the role of social and contextual factors in understanding women's vulnerability for risky sexual behavior in the context of drug use.
Financial Support: R01 DA19405

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CHOLINERGIC MODULATION OF REINFORCEMENT EFFECTS IN A REINSTATEMENT MODEL OF DRUG RELAPSE USING SUCROSE REWARD.

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Aims: This experiment explores the effects of rat cholinergic nucleus basalis magnocellularis lesions (NBM) on dopamine-dependent reward mechanisms in a reinstatement model of drug addiction and relapse using sucrose rewards. The finding of enhanced dopaminergic activation of the nucleus accumbens in the reward pathway in response to amphetamine treatment in rats with NBM lesions (Mattson et al., 2007) suggests that the DA response to sucrose reward will increase in NBM lesioned rats. Thus, NBM lesions were expected to increase sensitivity to sucrose in a sucrose-seeking reinstatement conditioning task.
Methods: After 192 IgG-saporin (n=12) or sham lesions (n=13) of the NBM, rats were trained in an operant sucrose-seeking reinstatement task. Rats were first shaped to press a lever for sucrose pellet before advancing to a variable ratio (VR-5) schedule. During VR-5 training, lever presses resulted in the presentation of an auditory-visual compound cue followed by sucrose delivery. After five days of training, operant behavior was extinguished across three days, where lever presses had no consequences. Finally, during the reinstatement phase, rats were reintroduced into the test chambers where lever presses only resulted in the presentation of the auditory-visual secondary reinforcer.
Results: The percentage of responding during the reinstatement phase relative to pre-extinction responding on the final day of VR-5 training was significantly greater in the NBM lesion group compared to sham lesion controls ($p<.05$).
Conclusions: Cortical cholinergic deficiency caused by selective immunotoxic lesions of the NBM led to an increase in operant responding for sucrose reward during cued reinstatement. Findings suggest that cholinergic interactions with the dopamine reward system may play a role in the processes associated with drug seeking and addiction. Low levels of cortical cholinergic function may predict vulnerability to drug addiction and relapse.
Financial Support: Funded by: MIDARP (R24DA025319)

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RELATIONSHIP BETWEEN OVERALL HEALTH AND COCAINE ABSTINENCE IN COCAINE AND ALCOHOL DEPENDENCE TREATMENT.

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Aims: Substance dependence can both cause new and exacerbate existing health problems, increasing the public health burden. As such, it seems important to examine overall health related outcomes in the context of substance abuse treatment. The SF-36 is a multi-purpose 36-question health survey that yields an 8-scale profile of functional health and well-being, and can be used to assess the health benefits produced by different treatments across several domains. Data from a recently completed double-blind placebo-controlled trial of Topiramate (TOP) for the treatment of combined cocaine and alcohol dependence ($n = 170$) were examined for health outcomes. Using the SF-36, as well as the cocaine use results from the study, this study sought to determine the relationship between treatment and health, as well as between cocaine abstinence and health.
Methods: The SF-36 was administered three times during the study; at baseline, at end of treatment and at follow-up. Urine drug screens were conducted thrice weekly for the entire 13-week trial.
Results: SF-36 scores increased significantly from baseline to end-of-study, and declined slightly from end-of-study to follow-up. There was no apparent relationship between baseline health and cocaine abstinence during the trial. However, cocaine abstinence during the study was predictive of improved health on the SF-36 at end of study among both placebo and TOP-treated subjects. Among TOP treated subjects, general health ($p = .001$), mental health ($p < .03$), vitality ($p < .02$), and physical functioning ($p < .04$), were correlated with abstinence in the last five, seven and nine weeks of treatment. Among placebo treated subjects, general health ($p < .04$), social functioning ($p < .008$), and emotional health ($p < .04$), were correlated with the same periods of abstinence.
Conclusions: These results suggest that health shows overall improvement as a function of cocaine abstinence, and that there is a relationship between treatment type and specific areas of health improvement.
Financial Support: Support for this study was provided by R01AA014657(KMK) and K01DA025073 (JGP)

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INTERACTION BETWEEN 5-HT2A RECEPTOR BLOCKADE AND 5-HT2C RECEPTOR ACTIVATION ON SPONTANEOUS AND COCAINE-INDUCED LOCOMOTION.

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Aims: Dopamine (DA) and serotonin (5-HT) play a role in locomotor activity in rats. The 5-HT2AR antagonist M100907 and the 5-HT2CR agonist MK212 have both been shown to attenuate cocaine-induced DA release and hyperlocomotion. To further understand the role of 5-HT2A and 5-HT2C receptors in these processes, this study sought to investigate the effects of administering a combination of M100907 and MK212 on locomotor activity. We hypothesized that 5-HT2AR blockade and 5-HT2CR activation may act synergistically, thus the two drugs would produce a greater effect together than when given alone.
Methods: We first established dose-effect functions for M100907 (0.0, 0.05, 0.075, 0.125, 0.25, or 0.5 mg/kg, s.c.) and MK212 (0.0, 0.125, 0.25, or 0.5 mg/kg, s.c.) on spontaneous locomotion in male rats (n=8/drug). Subthreshold doses (0.075 mg/kg M100907 and 0.125 mg/kg MK212) that had failed to alter locomotion on their own were then administered in combination to drug-naïve rats (n=11). We conducted a similar experiment to examine cocaine-induced locomotor activity, first establishing dose-effect functions for M100907 (0.025, 0.05 0.1, 0.2, 0.4 mg/kg, s.c.) and MK212 (0.125, 0.25, 0.5 mg/kg, s.c.) (n=8-11/dose). Subthreshold doses that failed to attenuate cocaine-induced locomotor activity on their own (0.05 mg/kg M100907 and 0.125 mg/kg MK212) were then co-administered as a cocktail to drug-naïve rats (n=24).
Results: For both spontaneous and cocaine-induced locomotion, only the drug combination significantly attenuated activity relative to vehicle, suggesting an interaction between 5-HT2AR blockade and 5-HT2CR activation.
Conclusions: It is likely that M100907 and MK212 produce this effect via a decrease in DA within the mesocorticolimbic pathway. Therefore, these findings are of particular interest as the M100907/MK212 treatment may attenuate behaviors associated with cocaine dependence, such as cocaine-induced hyperlocomotion and cocaine self-administration.
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PSYCHOLOGICAL FLEXIBILITY PREDICTS OPIOID MISUSE RISK IN LOW BACK PAIN PATIENTS RECEIVING OPIOID THERAPY.

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Aims: Opioid analgesic misuse (OAM) among chronic pain patients continues to be a significant public health concern. While OAM risk factors have been identified, e.g., history of a substance use disorder, there is scant research about cognitive and emotional processes that may drive OAM. Grounded in relational frame theory, psychological flexibility (PF) refers to an individual's capacity to change or persist in their behaviors, depending on the context and their goals and values. PF interventions are effective in improving chronic pain adaptation; however its association with OAM has not been investigated. This study examines the relationship between PF and current misuse risk.
Methods: We surveyed 119 patients receiving opioid therapy presenting with chronic low back pain at a pain management clinic. Participants had taken opioids for at least >19 days in the past month. The Brief Pain Inventory was used to obtain severity and interference scores. Psychological flexibility was assessed using: the Mindfulness Attention Awareness Scale (MAAS), the Chronic Pain Acceptance Questionnaire (CPAQ), and the Pain and Anxiety Symptom Scale (PASS). The Current Opioid Misuse Measure (COMM), a 17-item scale, assesses various aberrant drug-taking behaviors.
Results: Participants were 59% female and mean age was 49 years(SD 9.7). On a 0-10 scale, mean pain severity was 6.8(SD 1.8), and mean interference was 6.8(SD 2.3). Mean COMM score was 17.02 (SD 10.8) and 75% of participants COMM scores suggested elevated misuse risk. We fit a mutliple linear model controlling for age, pain severity and interference; CPAQ(β=-.14), MAAS(β=-.45), and PASS(β=.20) scores were significantly associated with COMM score (ΔR^2=.31). The full model predicted 45% of the variance in COMM [$F(6,112)=17.5$, $p<.0001$].
Conclusions: Results suggest that psychological flexibility may be important in understanding factors that contribute to OAM. To our knowledge, this is the first study establishing the association between psychological flexibility and opioid misuse.
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DEVELOPMENT AND IMMUNOLOGICAL VALIDATION OF AN OXYCODONE CONJUGATE VACCINE IN RATS.

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Aims: Opiate conjugate vaccines have shown promise in blunting the behavioral effects of heroin and morphine in rodent models. The goal of this study was to develop a conjugate vaccine against oxycodone, an increasingly abused prescription opiate.
Methods: Haptens were generated by adding functional groups and linkers at the 6 position of the oxycodone molecule. A series of haptens with linkers of various lengths was obtained by coupling oxycodone to an oligoglycine linker containing 0, 2, or 4 residues. An additional hapten was obtained by succinylation of oxycodone. Haptens were conjugated to carrier proteins by coupling available carboxyl groups to primary amines using a zero-length crosslinking agent. Promising conjugates were administered to rats for immunological screening.
Results: Hapten structure was confirmed by NMR and elemental analysis, while the efficiency of conjugation to carrier protein was determined by mass spectrometry. The best conjugation chemistry conditions had optimal molar hapten to protein ratios of 120 in acidic buffer. The most immunogenic conjugates had molar hapten to protein ratios of ≥10. Haptens containing the glycine(4) linker and conjugated to bovine serum albumin produced high serum oxycodone-specific antibody titers in rats as determined by ELISA. Competitive ELISA showed that serum antibodies were 1000-fold more potent in binding oxycodone than morphine or nicotine.
Conclusions: These findings show that this oxycodone conjugate vaccine is capable of producing high titers of oxycodone-specific antibody in rats. Use of the glycine(n) series provides a means of systematically investigating the effect of linker length on conjugation efficiency and conjugate immunogenicity.
Financial Support: Supported by NIDA grant DA026300 and a Career Development Award from the Minneapolis Medical Research Foundation

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EFFECT OF STRESS ON ATTENTIONAL BIAS AND COGNITION IN MARIJUANA-DEPENDENT INDIVIDUALS.

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Aims: Aims: Conditioned cues and negative affective states are implicated in drug use and relapse. How the distractibility of marijuana (MJ)-related cues or their influence on cognitive processes impact drug use, especially in stressful conditions, is unknown. The specific aims were to assess the impact of stress on MJ attentional bias (AB) and cognitive resources in MJ-dependent individuals (MJD).
Methods: Methods: MJD (n=19) and non-using controls (CON, n=13) were tested for AB (modified Addiction Stroop task, auditory odd-ball dual task procedure with MJ/control videos) and cognitive functioning (checkerboard task, digit-back task) pre and post a computerized stressor (PASAT-C); mixed-model ANOVAs and Pearson's correlations were used.
Results: Results: Although pre-stress AB scores and craving ratings in MJD were correlated ($r=0.60$, $p<0.01$), AB was not significantly different between groups and did not change differentially post-stressor. MJD had higher response errors than did CON on the dual-task procedure with a marginal differential improvement in performance during the MJ video vs. the control video post-stressor ($p=0.10$). MJD performed poorer than controls on the checkerboard task ($p=0.04$); both improved on the post-test ($p=0.05$). MJD performed much worse than CON before, but not after, the stressor on the digit-back task ($p=0.06$). Post-stressor craving ratings were not correlated with changes in AB or cognitive performance.
Conclusions: Conclusions: At baseline, MJD displayed deficits in attention, working memory and visual-spatial memory as compared to CON. Subsequent tests after an acute laboratory stressor resulted in greater performance improvement than CON on tests of attention and working memory in MJD, but did not increase MJ craving or AB. In contrast to what is seen with other drug use, acute stress may not lead to increased use or relapse to MJ-seeking behavior, nor impair practice effect on cognitive performance.
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HOW SUSCEPTIBLE IS THE ALCOHOLISM PROTECTION EFFECT OF ALDH2 EXON 12 SNP TO EPIDEMIOLOGIC VARIATIONS?

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Aims: We examine the relative strengths of association of ALDH2 exon 12 SNP with alcohol sensitivity, ethnicity and other indices using two Asian ethnic groups. The strong protective effect of the functional polymorphism (Lys487Glu) in Asian subgroups has been known for decades. Recent general-population epidemiologic survey results are often inconsistent with this genetic protection hypothesis. Mixed race Asians are at higher risk for substance abuse across classes of licit and illicit substances. These results indicate the protective effect of this SNP is still susceptible to environmental variations.
Methods: We interviewed 123 Japanese or Vietnamese residents ages 15 to 54. DNA samples were extracted from buccal brushes. Phenotypes were derived from self-reported use and selective DSM-IV symptom measures for alcohol, cigarette smoking, marijuana and any illicit drugs. Thirteen alcohol reaction items were assessed for one sip, one drink and 1+ drink. Both single (*2/*1 or 2*2) and double allele (2*2) effects were examined. Gender, ethnicity, mixed heritage, education, and income were entered in multivariate logistic analyses. We also used exact logistic regression which is suitable for a small sample size and to resolve an "empty" cell problem.
Results: ALDH2 genotypes differentiated alcohol reaction patterns. Acculturation and SES were associated with many alcohol and other substance use/abuse phenotypes. Beyond the powerful effect of *2/*2, a significant interaction was found for *2/*1 and gender with alcohol dependence syndrome but not with other phenotypes. Interaction between acculturation and genotypes was significant in multiple logistic but not in exact logistic.
Conclusions: Even with a small sample, the importance of main effects and interactions of genotypes with gender, ethnicity and potentially acculturation can be shown when a polymorphism has a large main effect. Such a study may be limited to "isolate" populations with high minor allele frequencies still being observed.
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HPA AXIS REACTIVITY TO SOCIAL STRESS AND ADOLESCENT CANNABIS USE:THE TRAILS STUDY.

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Aims: To investigate the relationship of lifetime and repeated cannabis use with hypothalamic–pituitary–adrenal (HPA) axis reactivity to social stress in a general population sample of adolescents. Adolescents who reported lifetime or repeated cannabis use, lifetime or repeated tobacco use, and never use of either cannabis or tobacco were compared with respect to their HPA axis reactivity.
Methods: The present study includes data from 591 adolescents (51% male) who participated in the GSST, which was an additional assessment during the third assessment wave of the TRacking Adolescents' Individual Lives Survey (TRAILS) study.
HPA axis stress reactivity was indexed by four cortisol samples collected before, during and after the GSST. Furthermore, all adolescents in our study completed self-reported questionnaires on lifetime and repeated cannabis and tobacco use. Models were adjusted for sex, recent alcohol use, experimental session risk status, socioeconomic status, mood, and time of the experimental session.
Results: Lifetime cannabis users had significantly lower stress reactivity levels when compared to abstainers (OR = 0.68, CI = 0.55-0.85, $p<0.01$) and lifetime tobacco users (OR = 0.79, CI = 0.64-0.98, $p<0.05$). In addition, repeated cannabis users also exhibited lower stress reactivity levels when compared to lifetime ever users of either tobacco or cannabis (OR = 0.74, CI = 0.53-0.98, $p<0.05$).
Conclusions: Lower HPA-axis stress reactivity in adolescents is specifically related to lifetime and repeated cannabis use.
Financial Support: Supported by the Netherlands Organization for Scientific Research (NWO) – Vidi scheme, Netherlands (452-06-004 to ACH and APvL)

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FACTOR STRUCTURE OF THE SPANISH VERSION OF THE CSSA IN PRIMARY COCAINE-DEPENDENT PATIENTS AND METHADONE-MAINTAINED COCAINE-DEPENDENT PATIENTS.

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Aims: To examine the factor structure of the Cocaine Selective Severity Assessment (CSSA) in primary cocaine-dependent patients and in methadone-maintained patients diagnosed with both heroin and cocaine dependence.
Methods: Chart review study aimed to collect the data about the CSSA filled out daily by the nursing staff. One of the daily CSSA was randomly chosen for exploratory factor analysis. Participants were 170 cocaine primary cocaine-dependent patients and 85 methadone-maintained cocaine-dependent patients all of them admitted for cocaine detoxification treatment.
Results: In the group of primary cocaine-dependent patients, the CSSA accounted for 62.2% of the total variance comprising five factors: 1) cocaine craving, negative mood, suicidality and paranoidism; 2) lethargy and hypersomnia; 3) carbohydrate craving and hyperfagia; 4) insomnia and hypofagia; 5) irritability and bradycardia. In the group of methadone-maintained patients, the CSSA accounted for 60.2% of the total variance comprising also five factors: 1) negative mood, irritability and lethargy; 2) cocaine and carbohydrate craving; 3) insomnia; 4) paranoidism and tachycardia; 5) hypofagia and suicidality.
Conclusions: The factor structure of CSSA found in primary cocaine-dependent patients is different from that found in cocaine-dependent methadone-maintained patients. Both factor structures of CSSA are clinically interpretable.
Financial Support: Supported by the Government Delegation for the National Drug Abuse Plan (Plan Nacional sobre Drogas) of Spain's Ministry of Health (Grant PND 2009/065) and, Department of Health of Catalonia Government.

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LOCOMOTOR ACTIVITY AND BEHAVIORAL STEREOTYPY DURING AN ESCALATING-DOSE "BINGE" PATTERN OF COCAINE ADMINISTRATION IN C57BL/6J MICE.

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Aims: We have shown that binge pattern cocaine results in significantly elevated levels of behavioral activity in C57BL/6J (C57) mice. The present study extends these findings by examining stereotypy and locomotor activity in the C57 mice during escalating-dose binge cocaine administration (EDCA), as well as withdrawal from and re-exposure to this regimen.
Methods: 10 male C57 mice were assigned to one of two treatment groups: 1) 14 days EDCA, followed by 14 days of withdrawal, followed by 14 days of another EDCA regimen, or 2) 14 days binge saline, 14 days withdrawal, 14 days binge saline. Mice received 3 daily injections of cocaine or saline at 1-hr intervals. In both 14-day EDCA regimens cocaine dose was started at 15 mg/kg/inj and increased by 5 mg/kg/inj every 3 days until a maximum of 30 mg/kg/inj was reached. Locomotor activity was monitored using an electronic monitoring frame and data was collected in 10-minute bins for 3 hours following the first daily injection. Total distance traveled, distance traveled in the cage periphery and center, and fine movements (stereotypy) were measured.
Results: EDCA resulted in a significant expression of stereotypy on all days of injections. EDCA also increased locomotor activity on all days of injections. On the first day of withdrawal locomotor activity was higher in cocaine treated animals than controls, which resolved by the third day. Cocaine treated animals showed thigmotaxis on all days of injections, which decreased during withdrawal.
Conclusions: EDCA results in expression of stereotypy and locomotor activity, without tolerance or sensitization. An earlier study of steady-dose binge cocaine administration to C57 mice showed tolerance to the locomotor stimulating effects of cocaine. This suggests that these models produce different behavioral profiles and possibly differential effects on neural pathways.
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STABILITY IN PRO-ABSTINENCE BEHAVIOR MEASURES: 18-YEARS FOLLOW-UP AFTER INTENSIVE 3-MONTH ALCOHOLISM TREATMENT PROGRAM.

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Aims: Using the concepts from Theory of Reasoned Action and Theory of Planned Behavior, different indicators of therapeutic success were studied to understand life style and pro–abstinence orientation during 18-years after-care period following a 3-months intensive alcoholism treatment.
Methods: The sample of 167 (128 male, 38 female) patients who started a 3-month intensive alcoholism treatment program has been followed-up for 18 years, using mailed standardized structured instruments. Data were collected before and at the end of the treatment, and in years 4-5, 9 and 18 of follow-up. The last data collection was completed by 32 subjects (26 males, 6 females) in 2010. Information on beliefs, behavioral intentions, normative behavior, life style and some demographic variables were selected for this analysis following standard explore-analyze-explore approach. After initial descriptive exploration of data, multivariate analysis of variance (MANOVA) was used to explore between-groups and within-groups differences over time.
Results: No robust differences were found between three time points after intensive treatment in self-perceptions, evaluation of own life style, perceived alcohol utility/harm, normative perceptions related to "social drinking" and readiness for open talk about dependence and help the others with their addiction problems.
Conclusions: The stability of pro-abstinence behavior indicators from 4-5 years after the end of intensive treatment up to 18 years of follow-up might suggest life-long changes. Longer longitudinal studies are needed to confirm this.
Financial Support: The study was supported by internal institutional resources.

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ACCEPTABILITY AND EFFICACY OF INTERNET-BASED CONTINGENCY MANAGEMENT TO PROMOTE SMOKING CESSATION.

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Aims: Contingency management (CM) increases abstinence from cigarette smoking by making vouchers contingent on negative carbon monoxide (CO) levels. To broaden the reach of CM, we developed an Internet-based CM intervention. The current study assessed the acceptability and efficacy of the intervention.
Methods: Smokers were randomly assigned to earn vouchers contingently (C; n =39) or noncontingently (NC; n = 38) on abstinence, verified by web-camera recorded CO samples submitted over a website. During the first 4 wks participants submitted 2 CO videos/day, and during the last 3 wks participants submitted 2 CO videos/wk. At the end of the 7-wk treatment, participants rated the program using a 100mm visual analog scale (higher scores were more favorable). Finally, participants returned to the lab 3- and 6-mos post-intervention to provide CO and self-reports of smoking.
Results: Participants in the C group submitted a greater percentage of negative CO samples (CO<=4ppm) during the intervention than participants in the NC group (C = 54%; NC = 35%; $t(75) = 2.10$ $P < 0.05$). Approximately 77% of the 4,774 scheduled CO videos were submitted. There were no group differences regarding the overall acceptability of the intervention (mean = 79.5). There also were no significant group differences in the percentage of abstinent participants at 3- (C = 23%, NC = 18%) or 6-mos (C = 13%, NC= 18%; based on 7-day point prevalence measures of CO <= 4ppm and self-reported abstinence).
Conclusions: Internet-based contingency management is effective at helping smokers initiate abstinence. Participants adhered at high rates to the 7-week intervention and rated the program favorably on a number of dimensions. However, complementary treatments may be necessary to promote long-term maintenance of treatment effects.
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POLY-DRUG AND MARIJUANA USE AMONG ADULTS WHO USE METHAMPHETAMINE.

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Aims: Research indicates that combining methamphetamine (meth) with other substances increases its risks and adverse health consequences. This study examines poly-drug and marijuana use in a sample of adults who used meth, and the association with health, mental health and criminal involvement.
Methods: Data (N=261) are from a 2009-10 follow-up interview in an intensive natural history study of adults who received treatment in 1995-1997 for meth abuse in Los Angeles county (n=169) and a comparison group of meth users who had not received treatment (n=92). Follow-up respondents who had not used illicit substances in the past year (41%) were compared to users of marijuana-only (n=16%), meth-only (n=9%), poly-drug users of marijuana and meth (15%), and heroin and/or cocaine with meth and/or marijuana (19%). Differences by drug use groups on demographics, mental health and criminal status were explored using chi square and GLM. Depressive symptomatology was measured using the Beck Depression Inventory.
Results: Preliminary analyses indicate women were more likely than men to use meth-only ($p<.05$). Fewer poly-drug users were employed (22-25%) compared to users of one drug (43-49%) and abstinent individuals (59%; $p<.001$). Higher depression scores were observed among poly-drug users (11.9-14.2) compared to the marijuana-only (7.3) and abstinent groups (8.1; $p<.001$). Those who used marijuana–only had the least number of arrests, convictions and incarcerations; e.g., the mean number of arrests in the past 8 years for marijuana-only users was 1.0, followed by 1.6 for the abstinent group, 3.7 for the meth-only group and 4.7-4.9 for the poly-drug use groups ($p<.001$). Multivariate analyses further examine the relationship of poly-drug use with substance use history and other factors.
Conclusions: Results suggest users of marijuana alone have comparable outcomes to those who were abstinent. However, meth users differed clinically and by criminal status depending on their recent use of other drugs, and these differences should be considered when planning treatment strategies.
Financial Support: NIDA DA025113

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BENEFITS OF TREATMENT DURING TREATMENT: ESTIMATING CONCURRENT EFFECTS.

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Aims: Background: Most substance abuse treatment programs are evaluated on outcomes at discharge or within a year following treatment, an approach that may miss important effects that occur during treatment.
Aim: To assess the effects of different modalities of care (outpatient, residential, both, or neither) on adolescent substance use, emotional problems, and illegal activities observed during the course of treatment.
Hypotheses: Both outpatient and residential treatments produce concurrent effects, though these effects differ by modality due to constrained opportunities to use drugs or engage in illegal behaviors when in residential treatment.
Methods: We use marginal structural models to estimate concurrent effects for 2870 adolescents receiving care in treatment programs funded by the Centers for Substance Abuse Treatment. Receipt of treatment and outcomes were assessed via retrospective client recall questions in the GAIN and were collected at intake and 3, 6, 9, and 12 months post intake.
Results: Adolescents have fewer substance use problems, on average, had they been receiving residential treatment versus had they been receiving no treatment (effect size (ES)=-0.13, $p<0.05$). Youth receiving both outpatient and residential treatment also report greater emotional problems than had they been receiving no treatment (residential ES: 0.25, $p<0.05$; Outpatient ES: 0.11, $p<0.05$). Youth receiving outpatient treatment also, on average, report more illegal activities than youth receiving no treatment (ES=0.06, $p<0.05$).
Conclusions: Youth receiving treatment have different outcomes than similar youth who were not. Differences include reduced substance use for residential treatment, increased criminal activities for outpatient treatment, and higher levels of emotional problems for either mode of treatment. These could be concurrent treatment effects or youth who are experiencing problems during a 90 period may turn to treatment creating spurious effects.
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YOUNG ADULTS' ANONYMOUS SELF REPORTS OF MARIJUANA USE ONLINE ARE RELIABLE AND VALID.

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Aims: Online surveys permit anonymity for self-reporting illegal behaviors such as drug use. This study examined the reliability and validity of self-reported marijuana (MJ) use online among young adults.
Methods: Participants were 1460 young adults age 18 to 25 across the US who completed an online survey anonymously. Over half (54%) had used MJ in the past 30 days. Measures included the Monitoring the Future MJ use items, 30-day timeline followback, the MJ consequences questionnaire, thoughts about MJ abstinence, MJ urges and temptations, MJ decisional balance, and nicotine and MJ interaction expectancies.
Results: Participants used MJ on average 9.0 days in the past 30. Measures of MJ use frequency, expectancies (alpha = .90), self-efficacy (alpha = .97), decisional balance (.95), and tobacco/marijuana interaction expectancies (alpha = .89) demonstrated high internal consistency reliability. In tests of convergent validity, past 30-day MJ use demonstrated significant associations with dependence symptoms (r=.37), MJ use expectancies (r=.48), desire to quit MJ use (r=-.33), expected success with quitting (r=-.32), expected difficulty with quitting (r=.33), and nicotine and MJ interaction expectancies (r=.26). In tests of divergent validity, past 30-day use did not correlate with measures of tobacco-related cognitions (all r's N.S.). In tests of concurrent criterion validity, MJ use distinguished groups that differed on MJ stage of change ($F=6.78$, $p<.01$) and abstinence goals ($F=8.04$, $p<.001$), but not demographic characteristics (age, gender, ethnicity, education, income). Prevalence of MJ use (54%) was higher in our study than that obtained from a nationally representative household interview among young adults (34%).
Conclusions: These findings generally support the reliability and validity of online assessment of marijuana use. Strategies to maximize the psychometrics of online surveys with young adults who use drugs are discussed.
Financial Support: P50 DA09253 and TRDRP #18-FT-0055

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PREDICTORS OF LEGAL PROBLEMS AMONG PATIENTS WITH BIPOLAR DISORDER AND ALCOHOLISM.

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Aims: Patients with comorbid bipolar disorder and alcoholism and other drug use represent a highly challenging clinical population. Many of these patients engage in illegal behavior; however, factors that predict illegal activities among this group are still unclear. The aim of this study is to examine predictors of legal problems among patients with comorbid bipolar disorder and alcoholism.
Methods: Fifty-two patients with DSM-IV/SCID comorbid diagnoses of bipolar I disorder and alcohol dependence were administered the Addiction Severity Index section on legal information every month for 6 months. The effect of alcohol use, drug use, bipolar subtype, gender, socioeconomic status, age, inpatient/outpatient recruitment, employed/unemployed, marital status, and significant familial support on the Addiction Severity Index score on legal problems was examined.
Results: Strongest predictors of the severity of legal problems were age 35 years or more ($t=-2.51$, $DF=29$, $p=0.02$) with an odds ratio of 14, inpatient recruitment ($t=2.50$, $DF=31$, $p=0.02$) with an odds ratio of 11, and single marital status ($t=2.50$, $DF=31$, $p=0.02$) with an odds ratio of 11. There was a trend for drug use to also predict legal problems ($t=-1.62$, $DF=14$, $p=0.12$) with an odds ratio of 3. Although not statistically significant, manic bipolar subtype, male gender, high socioeconomic status, employed, and lack of significant familial support also had higher means of legal problems severity scores.
Conclusions: These results suggest that age 35 years or more, inpatient recruitment, and single marital status among patients with bipolar disorder and alcoholism are predictors of higher severity of legal problems. Further studies are indicated to fully elucidate factors predicting legal problems in this population. These findings may have significant implications for the development of targeted preventative and treatment strategies.
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INDIVIDUAL DIFFERENCES IN THE LIKELIHOOD OF REBOUND INSOMNIA.

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Aims: While therapeutic hypnotic doses have not been associated with rebound insomnia, a worsened sleep relative to baseline following drug discontinuation, some individuals do show rebound. This study evaluated the reliability of producing rebound insomnia with repeated tests (i.e., placebo substitution) during 12 months of nightly use of zolpidem (10mg).
Methods: Primary insomniacs (N=16) ages 32-64, meeting DSM-IVR 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 10 mg zolpidem (n=16), double-blind, nightly for 12 months. On two laboratory nights in Months 1, 4, and 12 placebo was administered. Eight-hour sleep recordings were collected and rebound was assessed by comparing change in total sleep time from baseline on the two placebo subsitution nights.
Results: Within the zolpidem group, on both nights of month 1, 2 participants had shorter total sleep times (TST) than baseline. Their TSTs were consistently shorter than baseline both nights in months 4 and 12 ($F=7.22$, $p<.02$) than those with no month 1 rebound (n=9), or 1 night of rebound (n=3). The rebound did not worsen from month 4 to 12 (no nights or nights by drug interactions). One of the 2 was a female. Relative to the others (n=14), the 2 were similar in age (42 and 58 vs 52.3+11.2 yrs), but tended to have a shorter duration insomnia (7 and 10 vs 14.5+12.1 yrs) and to have better screening total sleep times (386 and 403 vs 351.8+38.5 min).
Conclusions: Twelve percent of insomniacs showed consistent rebound insomnia during placebo substitution of zolpidem (10 mg), which did not worsen from month 1 to 12, appearing to be a reliable individual difference in drug discontinuation response.
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THE EFFECT OF FAMILY FACTORS ON PRESCRIPTION STIMULANT USE IN YOUTH AGED 10-15.

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Aims: The National Monitoring of Adolescent Prescription Stimulant Study assesses prescription stimulant use among youth ages 10-18. Research findings on family structure and solidarity suggest association with adolescent drug use. This research focuses on the association between selected family factors and prescription stimulant use, predicting a higher number of positive family factors in youth who did not report non-medical use (NMU) of prescription stimulants.
Methods: N-MAPSS surveyed youth at entertainment venues in 10 metropolitan areas of the US. For this analysis, N-MAPSS participants aged 10-15 were selected and divided into three groups: lifetime non-users (NU) (n=2,515), past 30 day medical users (MU) (n=102), and past 30 day NMU (n=55). Any past 30 day non-oral use, use more than prescribed or use of an Rx stimulant that belonged to someone else was coded as NMU. Individuals who had used prescription stimulants prior to the past 30 days but were not current users were eliminated. The selected family factors were living situation, family dinners per week, and alcohol from a parent. Chi-square, t-tests and one-way ANOVA models were run with SAS v9.2.
Results: Mean age of the sample was 13.4±1.5; NMU were significantly older (13.8±1.3) than MU (13.0±1.6; $p=.001$). Significant differences among groups were found for living situation ($\chi2=9.6$; $df=4$; $p=.05$), number of dinners ($F=6.5$; $df=2$; $p=.002$), and alcohol from parent ($\chi2=15.0$; $df=2$; $p=.0006$). The mean number of positive family factors for the sample was 3.03±0.9 (mode=3); 36% of participants received maximum scale score of 4 for living with both parents, 4 or more dinners per week, and not getting alcohol from a parent. The ANOVA model was significant ($F=8.1$; $df=2$; $p<.0001$) with mean scale scores of NMU (2.56±1.03), MU (2.96±0.92) and NU (3.05±0.90).
Conclusions: We did find a higher number of positive family factors in youth who did not report NMU of prescription stimulants.
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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NICOTINE INHIBITS ESTROGEN SIGNALING AND INCREASES POST-ISCHEMIC HIPPOCAMPAL DAMAGE IN FEMALE RATS.

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Aims: Nicotine addiction is responsible for the elevated risk of cerebral ischemia (CI). CI causes delayed neuronal death in the hippocampal CA1 region. Here we hypothesize that a synergistic deleterious effect of nicotine and oral contraception (OC; NOC) exacerbates post-ischemic hippocampal damage in female rats.
Methods: To simulate smoking behavior-induced nicotine levels in the human body, we implanted osmotic pumps containing nicotine in the female rats for 16 days. Furthermore, we mimicked the use of oral contraceptives in females by administering oral contraceptives orally to the rat. Rats exposed to either nicotine alone or in combination with oral contraceptives were subjected to an episode of CI. CI was produced by 10 min of bilateral carotid occlusion and systemic hypotension (50 mmHg). Brains were examined for histopathology at 7 days of reperfusion.
Results: The data are expressed as a percentage of neuronal survival of the sham (saline-treated rats without CI). The number of normal neurons per section in the CA1 hippocampal region in sham rats was 1204 ± 105 (Mean±SD; n=6) and ischemic insult to saline-treated females at the proestrus stage decreased the normal neuronal count to 44% (525 ± 22, n=6; p< 0.001). Nicotine exposure followed by ischemic insult at the proestrus stage decreased the neuron count to 368 ± 56 (n=6), which amounted to 32% of normal neurons, as against sham. Oral contraceptive treatment alone did not have significant difference in the post-ischemic number of normal neurons (567 ± 21; n=6) as compared to saline group. Ischemic insult to NOC rats resulted in only 16% (197 ± 13; n=6) normal neurons as compared to sham. Interestingly, we observed a significant (p<0.001) difference in the post-ischemic number of normal neurons between nicotine alone and NOC group.
Conclusions: These results show that the synergistic deleterious effects of NOC exacerbate post-ischemic hippocampal damage as compared to nicotine alone in normally cycling female rats.
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SEX DIFFERENCES IN THE EFFECTS OF ORAL D-AMPHETAMINE ON IMPULSIVITY, MOOD AND PERFORMANCE IN NORMAL HEALTHY CONTROLS.

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Aims: Impulsivity is thought to be greater in males than females and d-amphetamine has been shown to decrease impulsivity in healthy individuals. However, it has yet to be determined whether there are sex differences in amphetamine's effects on a range of behavioral impulsivity tasks.
Methods: Males and females in the current study were carefully screened to exclude factors associated with increased impulsivity such as current alcohol or substance abuse, family histories of alcoholism or substance abuse, and all current Axis I disorders. To date, normal healthy males (N=17) and females (N=17; tested in the follicular phase of the menstrual cycle) were administered placebo or oral d-amphetamine (10 or 20 mg) during 3 outpatient sessions. Subjective measures of abuse liability, cognitive performance tasks, and behavioral measures of impulsivity and risk-taking were assessed at baseline and several times after drug administration each session.
Results: d-Amphetamine produced dose-dependent increases in ratings of Drug Liking and Stimulation in males and females; d-amphetamine increased Stimulation to a greater extent in males. There were no differences between males and females on the cognitive performance tasks and amphetamine did not improve performance in either group. There were no differences in scores on the Barratt Impulsivity Scale between males and females. 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). Males were more impulsive than females on the IMT and GoStop Task, but not on the DMT and DDT. However, d-amphetamine did not alter these impulsivity tasks in either group. Also, there was no difference between the groups or in response to d-amphetamine on the Balloon Analog Risk Task.
Conclusions: Overall, among a group of normal healthy individuals, males were more impulsive than females, and oral d-amphetamine did not decrease various impulsivity measures.
Financial Support: Supported by NIDA grants DA022282 (SCR), DA029647 (FRL) and DA009114 (SME).

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E-CIGARETTE ABUSE LIABILITY: SUBJECTIVE AND BEHAVIORAL EFFECTS OF SHORT-TERM SWITCHING.

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Aims: Electronic cigarettes (e-cig) have been promoted as a safer alternative for delivering nicotine to smokers. However, the appeal of e-cig may be limited compared with a conventional cigarette. Abuse liability of the e-cig among continuing smokers was assessed using a switching study design.
Methods: Participants (N= 41; 34.4 yrs of age; 68% male) were regular smokers not contemplating quitting, and were naïve to e-cig use. After a 72 hour baseline of usual brand of conventional cigarette use, subjects were switched for a further 10 days to a commercial e-cig product. Behavior was monitored throughout the study (smoking diary, phone interview) and follow-up lab sessions were conducted at Days 11 and 14. Puffing topography, smoking urges, nicotine withdrawal, sensory perceptions and drug effect and liking were measured pre- and post-smoking both products. Exposure to nicotine was assessed via salivary cotinine.
Results: After 14 days, conventional cigarette consumption declined from 14.6 cigarettes per day to 7.3 (p<.001). Subjects took larger (p=.045) and longer (p=.008) puffs when using the e-cig. E-cig use reduced negative urges to smoke after initial use (p=.029), 11 days (p=.04) and 14 days (p=.046) post switching. Smoking urge (p=.046) was reduced only at 14 days post switching. E-cig nicotine effect (p=.006) and liking (p<.001)were rated significantly lower than the conventional cigarette.
Conclusions: E-cigarette use reduced smoking urges and withdrawal, and overall conventional cigarette use, but nicotine effect and liking responses suggested a less optimal e-cig nicotine reward. Complete substitution for conventional cigarette use did not occur with e-cigarettes, further suggesting limited consumer appeal. These data suggest that e-cigarettes are likely to be used dually with conventional cigarettes, resulting in no reduction in nicotine dependence, nor in exposure to tobacco toxicants. The implications of these findings for regulatory policy by the FDA and other agencies will be discussed.
Financial Support: National Cancer Institute grant # RO1CA125224

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CAFFEINE-PRIMED REINSTATEMENT OF COCAINE-SEEKING BEHAVIOR IN RATS SELECTED FOR HIGH AND LOW IMPULSIVITY.

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Aims: High impulsive (HiI) rats exhibit greater amounts of cocaine-seeking behavior compared to low impulsive (LoI) rats across several phases of the drug abuse process. However, no studies have investigated the potentially differential effects of stress-induced reinstatement of cocaine seeking and its treatment in these two groups. In previous studies, allopregnanolone (ALLO) was used to reduce cocaine-seeking behavior. The purpose of this study was to compare HiI and LoI rats on drug- [cocaine (COC) and an aversive dose of caffeine (CAFF)] and stress- [yohimbine (YOH)] primed reinstatement of cocaine seeking behavior, comparing treatment effects of ALLO on these measures.
Methods: Rats were selected for either high (HiI) or low (LoI) impulsivity using a delay-discounting task. They were then trained to lever press for cocaine (0.4 mg/kg) under a FR 1 schedule during daily 2 h sessions. Following a 12-day maintenance period cocaine was replaced with saline, and rats extinguished lever pressing. Rats were then administered priming injections of saline, COC (15 mg/kg), ALLO (15 mg/kg) + COC, YOH (2.5 mg/kg), ALLO + YOH, CAFF (40 mg/kg), or ALLO + CAFF on separate days.
Results: There were no differences between the HiI and LoI rats for saline-, COC-, or YOH- induced reinstatement. In contrast, LoI rats showed higher CAFF-induced reinstatement compared to HiI rats. In addition, ALLO attenuated COC- and CAFF- induced reinstatement in the LoI rats but not HiI rats. However, ALLO failed to block YOH-induced reinstatement in both groups.
Conclusions: The results suggest that individuals who are less impulsive may have greater success with some pharmacological interventions for cocaine-seeking, but they could also be more susceptible to aversive events that lead to relapse.
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METHAMPHETAMINE SELF-ADMINISTRATION IN FEMALE RATS.

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Aims: Methamphetamine (meth) is a potent and addictive stimulant that can have long-term health consequences. Gender differences occur in the epidemiology of meth addiction, meth pharmacokinetics and pharmacodynamics, and treatment response outcomes. However, animal models of meth addiction and relapse have not been extensively characterized in female rats. Here we describe meth self-administration (SA) and reinstatement in freely cycling female rats under limited daily meth conditions.
Methods: Long-Evans female rats self-administered i.v. meth (0.0175 mg/infusion) on an FR1 schedule of reinforcement (21 days) in daily sessions. Each infusion was accompanied by a discrete light and tone stimulus complex. We examined responding in the absence of reinforcement when rats were returned to the drug context following a period of abstinence (i.e., context relapse), and following daily extinction trials (i.e., cue-induced and meth primed reinstatement).
Results: Female rats readily acquired meth SA, with an average daily meth intake of (mean ± SEM) 1.03 ± 0.04 mg/kg meth. Total meth intake across the 21 days of SA was 21 ± 0.87 mg/kg. Escalation of meth intake was not apparent nor did estrous cycle influence drug intake during 1-hr/day limited access. Rats showed robust meth-seeking as measured by lever pressing after abstinence (context relapse test, 85.6 ± 12.5) and during cue-induced reinstatement after extinction (97.0 ± 20.3). Additionally, female rats showed dose dependent reinstatement to meth priming injections (0.03-3 mg/kg), with doses of 0.3 (127.5 ± 38.5) and 1 (102.7 ± 17.7) mg/kg robustly increasing meth-seeking.
Conclusions: Relative to our prior results in male rats, females acquire meth SA faster and show more robust reinstatement to both meth-associated cues and meth-priming injections. Thus far, we have demonstrated that female rats are more sensitive to meth relative to males during acquisition and relapse testing. Ongoing experiments will determine whether female rats escalate meth intake and show altered reinstatement after more prolonged daily meth access in a manner similar to male rats.
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VULNERABILITY FOR SUD, DRUG USE AND RISK FOR VIOLENT BEHAVIOR.

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Aims: This study examines childhood transmissible risk for SUD as it covaries with number of different types of violent offenses, amplified by alcohol and marijuana use. The hypotheses for this study are: 1) Transmissible liability for SUD is a direct predictor of number of violent offenses manifest by young adulthood; 2) Acceleration of alcohol and marijuana use during adolescence is a mediator of the association between transmissible risk for SUD and number of violent offenses; and, 3) Boys are more likely than girls to commit violent offenses controlling for severity of transmissible SUD risk.
Methods: A sample of 359 subjects was prospectively followed from age 10-12 to age 22. Measures of alcohol and marijuana use frequency and the transmissible liability index (TLI) were conducted at 5 timepoints. The outcome was number of violent offenses committed by age 22. Parallel latent growth curve analysis with a continuous outcome was conducted to model the trajectory of marijuana use and alcohol use between ages 10-12 and 22 taking into account severity of the individual's transmissible liability at baseline and gender.
Results: Lifetime history of violent offenses is predicted by rate of marijuana use (b=1.25, z=3.81, p<.001), acceleration of marijuana use (b=.67, z=5.28, p<.001) and TLI (b=.10, z=2.19, p=.03. Slope and quadratic term of marijuana use mediates the association between TLI and violent offenses (b=.22, z=2.71, p=.007; b=-.09, z=-2.64, p=.008). The association between gender and number of violent offenses is mediated by slope (b=.72, z=2.78, p=.005) and acceleration of marijuana use between ages 10-12 and 22 (b=-.25, z=-4.294, p<.001).
Conclusions: Transmissible liability index (TLI) at age 10-12 predicted number of different types of violent offenses committed up to age 22 in both genders. Frequency of marijuana use, but not alcohol consumption, is a predictor of violent offending. The slope reflecting rate of increase in frequency of marijuana use between 10 and 22 years of age mediates the association between transmissible risk and number of different types of violent offenses.
Financial Support: NIH Grant # 2 P50 DA005605

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LONGITUDINAL CHANGES IN THE SOCIAL NETWORKS OF DRUG-USING PROBATIONERS.

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Aims: This study uses data from a randomized trial of probationers, to examine how the characteristics of their social networks change over a 12 month period in response to the study intervention and patterns of drug use.
Methods: A total of 250 subjects were recruited at baseline, with follow up rates at 97% for 3 months, 94% for 6 months and 90% for 12 months. Data from the Orientation of Social Support (OSS) form was used to determine the characteristics of the networks including the size and percent of family members.
Results: The number of persons reported in a subject's drug use network declined over time, from an average of 4 persons at baseline to an average of 2 at the 12 month follow up. Those in the intervention group who were polydrug users at baseline (40% of the overall sample) had decreases in their drug using networks over time compared to polydrug users in the control group (1 person vs. 2 persons at 12 months, $p < .05$). Polydrug users had more persons in their drug using networks at the 3 month follow up than those who used only one drug. Those with a high risk for recidivism had fewer persons who accepted them at baseline, compared to those with a moderate risk (4 vs. 5, $p < .01$), and also fewer persons who opposed their criminal activity (3 vs. 4, $p < .05$). This trend continued at the 3 month follow up but not at the 6 and 12 month follow ups.
Conclusions: The intervention appears to have decreased drug using networks for those who were polydrug users, although all probationers in the study decreased their drug using networks, indicating that community supervision may help to change negative network influences for offenders, including those at high risk for recidivism. Polydrug users are often a problematic group, so this intervention, focused on combining treatment with supervision, may provide useful tools for this population.
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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STRENGTH OF ASSOCIATION BETWEEN TWO RODENT MODELS OF IMPULSIVITY AND COCAINE SELF-ADMINISTRATION.

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Aims: Impulsivity, broadly defined, refers to factors that regulate expression of inappropriate or maladaptive behaviors. Two behavioral processes thought to underlie behavioral regulation are response inhibition and delay discounting. Here, we examined the association between response inhibition (measured using a stop task), delay discounting (using an adjusting amount procedure) and cocaine self-administration (SA) in rats.
Methods: Data were obtained from 44 rats trained on the Stop Task (For a description of the task, see Feola, et al., Behav. Neuroscience, 114, 838-834, 2000.) and 24 rats trained on a Delay Discounting (For a description of the task, see Richards et al., JEAB, 67, 353-366, 1997.). On the delay discounting task, rats were trained with 3 delays to reward: 0, 4, & 12 s. At the end of testing, rats were fitted with chronic indwelling jugular catheters and tested for 5 days for acquisition of a low dose of cocaine SA (0.3 mg/kg/inf). Infusions of cocaine were available according to a fixed ratio 1 schedule of reinforcement followed by a 30 s time-out period.
Results: Stop Task: The correlation between stop reaction time and cocaine SA was not significant ($r = 0.25$). However significant correlations were obtained between Go reaction time ($r = 0.38$) and premature responses ($r = 0.37$) and cocaine SA. Delay Discounting: Area under the discount curve was significantly correlated with cocaine SA ($r = 0.44$). Indifference points obtained at the 4 s ($r = 0.42$) and 12 s ($r = 0.41$) delays were significantly correlated with cocaine SA while indifference points obtained at 0 s ($r = 0.04$) were not.
Conclusions: These results indicate that performance on both the stop task and delay discounting task are associated with acquisition of cocaine SA. Delay discounting may be a stronger predicator than the stop task.
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HPA AXIS RESPONSE TO STRESS PREDICTS DISTRESS TOLERANCE AMONG COCAINE USERS.

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Aims: Negative reinforcement theories emphasize that the motivational basis of addictive drug use is the reduction or avoidance of negative states. Recent behavioral studies of distress tolerance (DT), defined as the ability to persist in goal directed behavior in the face of affective distress, have provided support for negative reinforcement processes in substance use outcomes, such that low DT is associated with shorter abstinence durations and increased risk of treatment dropout among substance users. Although the negative outcomes associated with DT are well established, the mechanisms underlying DT are less clear. One mechanism of interest is the HPA axis and its primary hormone, cortisol. Chronic drug use is associated with allostatic changes in HPA axis functioning, and cortisol reactivity to stress is associated with substance use outcomes across drug classes. Despite the theoretical link, empirical evidence of the association between DT and HPA axis functioning among substance users is lacking. Thus, the aim of the current study was to examine the association between DT and HPA reactivity to stress in a sample of 14 cocaine-dependent individuals in residential treatment.
Methods: Participants completed a computerized DT task (PASAT) with DT measured as latency in seconds to task termination. On a separate testing day, they completed the PASAT again for a standardized length of time, and provided salivary cortisol samples immediately before the task, and every ten minutes thereafter for a total of 40 minutes post-task.
Results: Linear regression analyses indicated that peak cortisol response to the PASAT was associated with DT such that lower peak cortisol response to stress was associated with low DT, above and beyond the effects of self-reported distress and skill on the task ($p = .049$). The overall model accounted for 49.9% of the variance in DT.
Conclusions: Findings suggest that cocaine users who display blunted HPA axis reactivity to psychological stress may be most vulnerable to negative reinforcement behaviors.
Financial Support: NIDA1F31DA027242-01A1 (PI: Richards)

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PATTERNS OF PRESCRIPTION MEDICATION DIVERSION AMONG DRUG DEALERS.

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Aims: The diversion of controlled medications is a serious public health problem that continues to drive the prescription drug abuse epidemic. While prior studies confirm that dealers are a major supplier of diverted medications to the black market, knowledge regarding how dealers acquire these medications is limited. This research aims to respond to the frequently cited need for additional data on the diversion activities of dealers. The following research questions were posed: 1) how do drug dealers acquire their inventory of prescription medications? and 2) which types of prescription medications do dealers most commonly sell?
Methods: Data are drawn from a large 4-year NIDA funded research study which examined prescription drug diversion and abuse in South Florida. In-depth semi-structured interviews (n=50) were conducted with an ethnically diverse sample of prescription drug dealers from a variety of milieus to assess patterns of diversion. Audiotapes of the in-depth interviews were transcribed and thematically analyzed using the NVivo 8 software program.
Results: Dealers relied on a wide array of diversion methods including visiting multiple pain clinics, working with pharmacy employees to smuggle medications from pharmacies, and purchasing medications from indigent patients. Dealers also engaged in various forms of fraud related to Medicare, Medicaid, and other types of health insurance. The type of medication most commonly sold by dealers was prescription opioid analgesics, and to a lesser extent benzodiazepines such as alprazolam.
Conclusions: These findings inform public health policy makers, criminal justice officials, the pharmaceutical industry, and government regulatory agencies in their efforts to reduce the availability of diverted prescription drugs in the black market. Specifically, these data seem to support the need for a statewide prescription drug monitoring program and increased regulation among pain clinics and pharmacies.
Financial Support: This research was supported by NIH Grant Number R01DA021330 from NIDA.

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NICOTINE PREEXPOSURE IN ADULTHOOD ALTERS THE AVERSIVE, PHYSIOLOGICAL AND REINFORCING EFFECTS OF ALCOHOL.

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Aims: The aversive effects of drugs of abuse likely serve to limit intake (and abuse potential) and can be modulated by a number of factors (including drug history). The following studies examined the impact of a history with nicotine (NIC) on the aversive, physiological and reinforcing effects of alcohol (EtOH) in adult rats.
Methods: In Experiment 1, rats were given 10 daily injections (IP) of either 0.4 mg/kg NIC (n=32) or saline (SAL, n=32) from postnatal (PND) 70 to 79. Six weeks later, they were given taste aversion conditioning in which saccharin was paired with varying doses of EtOH (0, 0.56, 1.0 or 1.8 g/kg, IP). Hypothermia and BACs were also assessed. In Experiment 2, similarly preexposed animals (NIC, n=21 or SAL, n=21) were assessed for changes to the reinforcing effects of EtOH. Six weeks following preexposure, animals were assigned to receive 2-h access to saccharin alone or saccharin + EtOH (that increased in concentration from 1 to 5% over sessions). Animals were given 1-week access to each concentration. BACs were assessed following the final session of fluid access.
Results: In Experiment 1, NIC preexposure significantly attenuated the aversive effects of EtOH (1.8 g/kg, $p < 0.05$) as well as attenuated EtOH-induced hypothermia (1.8 g/kg, $p < 0.05$). BACs were not impacted. Analysis of the mean of the last 3 days of consumption for each week of Experiment 2 revealed that there was no effect of NIC preexposure on either H2O or saccharin consumption, but NIC preexposure significantly increased consumption of the saccharin + EtOH solution at all concentrations of EtOH ($p < 0.05$), although this was not reflected in BACs.
Conclusions: These data demonstrate that a history of NIC attenuates the aversive and hypothermic effects of EtOH and increases EtOH consumption later in life, potentially impacting its risk for abuse. These data further implicate a role of nAChRs in the affective and reinforcing effects of EtOH.
Financial Support: Supported by a grant from the Mellon Foundation to ALR and extramural funds from NIAAA/NIH.

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THE RELATIONSHIP BETWEEN DRUG USE AND THE BUSINESS CYCLE: POTENTIAL IMPLICATIONS OF THE GLOBAL FINANCIAL CRISIS.

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Aims: The literature on alcohol use and business cycles suggests that higher unemployment rates and recessions result in lower alcohol consumption and harms, notwithstanding some complexity around regular versus occasional drinkers. Examination of the relationship between business cycles and drug use has been barely studied. We sought to explore the relationship between the Australian business cycle and drug use and frequency of use.
Methods: Using individual level data from seven repeated cross-sections of Australia's National Drug Strategy Household Survey (NDSHS), spanning 1991 to 2007, this study examined the relationship between illicit drug use of Australians aged 14 to 49 years and the unemployment rate and income per capita, two indicators of the business cycle. Analyses of the impact of gender and age are conducted.
Results: Last year drug use decreased as the unemployment rate increased. For those that were already using cannabis the frequency of use was not significantly related to either the unemployment rate or income per capita. This suggests that existing users are insensitive to the business cycle but participation in use is sensitive. The population wide findings do not necessarily hold for all men and women. While young women's participation in drug use is reduced with rising unemployment rates, the drug use of men younger than 35 is unresponsive. The results for income per capita are less clear: the participation of older men and women increases with declines in income per capita.
Conclusions: The rise in unemployment rates associated with the financial crisis may result in fewer young Australians using illicit drugs, but little change in those that already use drugs. However, falls in per-capita income may increase the number of older Australians using illicit drugs.
Financial Support: Colonial Foundation Trust

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FACTORS ASSOCIATED WITH THE LEVEL OF KNOWLEDGE ABOUT METHADONE TREATMENT IN THE SENTENCED POPULATION OF THE PUERTO RICAN PRISON SYSTEM.

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Aims: PR has a large number of individuals with opioid dependence under the supervision of the correctional system. There is a large Medication Assisted Treatment(MAT)gap both in prision and community. Client's knowledge about opiate dependence and its treatment are predictors of treatment success.Knowledge can contribute to treatment adherence in those who are ready. We explore: the extent of knowledge about methadone as a treatment modality for opioid dependence among prison inmates in the PR prison system and the variables that explain it; if knowledge predicts a preference for MAT compared with drug free treatment modalities among inmates with opiate dependence.
Methods: Cross sectional anonymous survey in 2005 with a representative sample of sentenced male & female inmates of the Puerto Rican correctional institutions approved by the IRB. Structured interviews were used: Computer Assisted Personal Interview, assessing social and health variables and diagnosis of drug abuse/dependence and Audio Computer Assisted Self Interview for sensitive information related to the use of illicit drugs and risky behaviors in and outside of prison. Knowledge of MAT is measured with a 10 item subscale adapted from the validated Spanish version of Caplehorn, et al. Scale (1996) designed to measure knowledge and attitudes towards methadone.
Results: A total of 1,179 individuals participated in the study (89% response rate). 66% of the general prison population regardless of whether or not the respondent fulfilled a Substance Use Disorder(SUD)diagnosis had medium or high knowledge of Methadone treatment. Among those with a SUD, 301(31%)of male and 89(40%)of female inmates attained knowledge scores within this range. We will report the variables predicting knowledge level and the association between knowledge and treatment modality preferences adjusted for other correlates.
Conclusions: Findings will inform effforts by the prison health authorities to enhance the acceptability of MAT and engage inmates with opiate dependence in treatment as part of a pre-release program.
Financial Support: No

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ADOLESCENT MALE AND FEMALE RATS SHOW ENHANCED RESPONDING TO SUCROSE REWARD IN A PAVLOVIAN CONDITIONING PARADIGM.

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Aims: Adolescents, who are particularly vulnerable to drug abuse and addiction, differ from adults in their sensitivity to reward. It is unclear how they differ and if there are sex differences in reward processing. Here, we studied these issues by training adolescent and adult rats in a Pavlovian conditioning paradigm where a conditioned stimulus (CS) was paired with delivery of a 20% sucrose solution.
Methods: Male and female Sprague-Dawley rats were food-restricted and began training in adolescence (postnatal day (P) 34) or adulthood (P102). For 8 daily sessions, rats were given 8 CS+ (tone) trials that were followed by sucrose delivery and a 90-150s ITI. These were interspersed randomly with 8 CS- (light) trials. Prior to the ninth session, the effect of outcome devaluation (OD) on conditioned behavior was tested by providing the rats with 1hr free access to sucrose. This was followed by 2 more training sessions and 5 days of twice-daily extinction sessions. Lastly, re-acquisition of conditioning was assessed in 2 training sessions.
Results: Preliminary data indicate that during conditioning, both male and female adolescents had relatively more sucrose trough entries during the CS+, compared to adults; at the same time, female adults had more CS+ entries than male adults. During OD, there were no age-dependent differences, though females at both ages devalued less than males. In adults, this occurred even though females drank more sucrose than males during free access. There were no age or sex differences in extinction, but adolescents of both sexes exhibited greater re-acquisition.
Conclusions: These results suggest that both male and female adolescent rats are hyper-responsive to reward and associated cues, compared to adults. Females at both ages are also more responsive to reward and less sensitive to devaluation. In future studies, we will determine the role of age-dependent differences in prefrontal cortex dopamine and NMDA receptor function in these effects.
Financial Support: UIUC Neurosci. Prog. Fellowship

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INDIVIDUALS WITH HIGH ATTENTIONAL BIAS FOR COCAINE CUES AND BLUNTED MOTIVATION FOR NON-DRUG REWARDS MAY BE AT RISK FOR LONG-TERM COCAINE USE.

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Aims: Cue reactivity is considered an important component of drug dependence. The cocaine Stroop task has been used to assess automatic attention capture by cocaine cues (attentional bias). A number of factors may moderate associations between attentional bias and drug use. The relationship should be stronger in individuals who have blunted motivation for non-drug (e.g., monetary) rewards because individuals with high motivation can gain alternative reinforcement from non-drug rewards.
Methods: We tested this moderator hypothesis in participants (N=89) enrolled in a clinical trial examining the effect of levodopa on treatment of cocaine dependence. At baseline, participants completed a cocaine Stroop task and an experimental task of motivation, the progressive ratio reinforcement schedule (PR).
Results: On the Addiction Severity Index participants reported using cocaine on 14.7 (SD = 9.2) of the past 30 days (recent use). They reported using cocaine for 15.3 years (SD = 7.6) (lifetime use). Overall, participants exhibited a large cocaine Stroop effect (M = 57.6 ms, d = 0.83). For lifetime (but not recent) use, using ANOVA there was an interaction between the (dichotomized) Stroop and (dichotomized) PR responses ($p < .05$). In individuals with low motivation, lifetime use was greater in individuals with high (vs. low) cocaine Stroop effects ($p < .05$).
Conclusions: Attentional bias was more strongly associated with reported past use in individuals with lower motivation. Individuals with high attentional bias and blunted motivation may be at risk for long term cocaine use. These individuals may benefit from treatment approaches that target both attentional bias and blunted motivation.
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ALCOHOL AND DRUG TREATMENT OUTCOME STUDIES METHODOLOGICAL REVIEW (2005-2010).

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Aims: To assess the methodological quality of both alcohol and drug treatment outcomes for studies published within the years 2005-2010.
Methods: For inclusion purposes, studies had to meet criteria including published in a peer-reviewed, English-language journal between the years 2005-2010; not a primary care or detoxification-only study; study subjects had to have had a primary alcohol or primary drug use diagnosis not a case or multiple-case study; and presented treatment outcome data for a minimum follow-up interval of 3 months. Studies were then evaluated with respect to reporting: demographic variables; pretreatment drug use variables; study variables; treatment variables; and follow-up variables.
Results: Of the 31 studies reviewed, the majority (74.2 %) reported ethnic and racial demographics, roughly a quarter reported income data (25.8%), almost half did not report employment status. Only 50% used established diagnostic criteria (e.g., DSM-IV). Less than a quarter of reported the length of an individual's alcohol problem (17.4%), a similar number reported prior history of alcohol related hospitalizations (17.4 %), and a third (33.3%) reported whether prior treatment for alcohol problems had occurred. While all studies reported randomization, less than two thirds provided specific methods of randomization (66.7%). In terms of follow up intervals, 50% reported a follow up interval of 12 months, followed by 6 months (16.7%) and 3 months (10%). Although the vast majority of studies reported at least some findings of statistical significance, only two thirds (66.7%) reported effect sizes.
Conclusions: Methodological shortcomings are apparent both within and across studies. While advancements are evident, there are still important inconsistencies and limitations across treatment outcome research studies in the substance use field. Future studies should take these factors into account to improve the methodological quality within studies and facilitate drawing comparisons between studies.
Financial Support: No financial support or funding provided

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SEX DIFFERENCES IN HPA AXIS RESPONSE TO NALTREXONE: PRELIMINARY EVIDENCE FOR THE INFLUENCE OF ESTRADIOL.

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Aims: Our laboratory has previously demonstrated that naltrexone, a mu-opioid receptor antagonist, increases HPA axis hormone release (i.e., ACTH and cortisol) to a greater extent in women smokers than in men. We have also found preliminary evidence that self-reported menstrual cycle (MC) phase may impact women's response to naltrexone. The aim of this study was to extend these initial findings by examining if estradiol (E2) level affects HPA axis response to naltrexone in women smokers.
Methods: Sixteen women smokers were tested in two separate morning sessions after an overnight CRC stay. At 8:00am, each participant received 50 mg naltrexone or placebo capsule in random order. Blood samples were obtained over the next four hours to measure ACTH and cortisol response. Samples were also assayed for E2 and progesterone levels, which were used to confirm participants' self-reported MC phase for each session (e.g., based on date of last menstruation, cycle length, and reproductive phase). Thirteen of the sixteen women had MC phases that were objectively verified by E2 and progesterone levels. The three women who could not be verified were excluded from analysis. In the naltrexone session, women who were in the early follicular phase of the MC or were post-menopausal/-hysterectomy were classified as low E2 (n=7). Women who were in the late-follicular or mid-luteal phase were classified as high E2 (n=6).
Results: Women with a low E2 level had significantly greater ACTH and cortisol response (Drug*E2 Level, p's<0.05) to naltrexone than women at a high E2 level.
Conclusions: The results of this study provide preliminary evidence for E2 level as a potential factor underlying sex differences in response to naltrexone. If these findings are supported in a larger E2-controlled study, they may have implications for treatment of addiction with naltrexone and for pharmacological studies administering drugs that act on mu-opioid receptors.
Financial Support: This research was supported by NIH grants (R01-DA016834, K08-AA00276, F31-AA15017) and a NCI Cancer Center Grant (P30-CA14599).

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AN ECONOMIC AND ETHNOGRAPHIC INVESTIGATION OF FRESH START (DETROIT).

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Aims: Aim 1: Use ethnographic interviews, social network analysis and economic surveys to describe contexts and outcomes of urban female, drug-using sex workers at each phase of court-ordered drug treatment and recovery process. Aim 2: Describe patterns and pathways that women follow through the Fresh Start Project and develop an index of behavior change across program phases. Aim 3: Examine the role that social network ties and sociospatial contexts play in producing economic outcomes. The long-term goal of this pilot work is to develop interdisciplinary methods for a larger, longitudinal study to explore factors related to recovery.
Methods: In this cross-sectional study, economic and ethnographic interviews take place with 30 women from each phase of the program: incarceration, treatment, and graduation (n=90). In addition, interviews from 10 women who have terminated are planned for a total of 100 interviews.
Results: Interviews of both active and retired sex workers are ongoing (n=52 of planned 100). The first subgroup of active prostitutes (n=14) reports average monthly income of $6046 from sex work and spending 83% of total monthly income on drugs. They average 73 dates per week; 8 report heroin and 5 report crack as primary drug. In a second subgroup (n=13) interviewed during treatment, none report active drug use or sex work, mean monthly income is $400 and three report employment. In a third subgroup of 21 program graduates, mean monthly income is $884 and one reports active drug use. Interviews with four who have terminated the program are complete; two report active drug use.
Conclusions: Phases of recovery for participants in the Fresh Start Project can be described using social network and economic descriptors. As women are removed from street life, their incomes, expenditures and networks are reduced drastically and expand slowly after graduation. While earnings and expenditure profiles never fully reach the previous levels of active street life, expenditures are drastically reduced due to the elimination of drug expenditures.
Financial Support: NIH NIDA 1 R21 DA027145-01

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NOVELTY-SEEKING CORRELATES WITH A STRONGER RESPONSE OF ADOLESCENT MICE TO THE REWARDING PROPERTIES OF COCAINE IN THE CONDITIONED PLACE PREFERENCE PROCEDURE.

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Aims: Aim: The aim of the present study was to evaluate if performance in the hole-board test can predict a higher response to the conditioned rewarding effects of a subthreshold dose of cocaine (1 mg/kg) in a conditioned place preference (CPP) assay, and if there is a correlation with level of anxiety in the elevated plus maze (EPM).
Methods: Methods: Adolescent (PND 28, n= 47) and adult (PND 80, n= 46) OF1 mice were employed. All procedures involving the mice and their care complied with national, regional and local laws and regulations, and with European Community Council Directives (86/609/EEC, 24 November 1986).Statistical analyses: The CPP data for adolescent and adult mice were analyzed using a mixed ANOVA with two between variables (Age and Novelty seeking) and a within variable Days with two levels. A t-test and Pearson correlation were used to compare the results for adult and adolescent animals in the hole-board and elevated plus maze.
Results: Results: There was a correlation between number of DIPS and time spent in the open arms only among adolescent mice, higher number of DIPS correlates with more time spent in the open arms of the EPM (p> 0.02). Only high novelty seekers developed cocaine CPP. Also, only among adolescent high novelty seekers there was a correlation between the number of DIPS and an increase in the time spent in the drug-paired compartment.
Conclusions: Conclusions: Our results suggest that a "vulnerable" phenotype that predisposes subjects to cocaine reward can be predicted by novelty seeking, evaluated with the Hole-Board test, specifically in adolescent animals, and less so in adult animals.
Financial Support: Supported by: Ministerio de Ciencia e Innovación. Dirección General de Investigación (PSI2008-00101/PSIC), Instituto de Salud "Carlos III" (FIS), RETICS, Red de Trastornos Adictivos (RD06/001/0016) and Generalitat Valenciana, Conselleria de Educación (PROMETEO/2009/072), Spain.

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AN EXAMINATION OF SELF-STIGMA IN SCHIZOPHRENIC PATIENTS WITH A SUBSTANCE ABUSE DISORDER.

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Aims: The current study examined the role of self-stigma, or negative reactions toward the self as a result of being a member of a stigmatized group, in individuals with co-occurring schizophrenia and substance abuse. Specifically, the study explored the relationship between psychosis and addiction severity as it affects self-esteem and self-efficacy. Perceived dangerousness, stereotype awareness, and stereotype concurrence were hypothesized to mediate self-stigma formation.
Methods: Forty-nine participants with co-occurring schizophrenia and substance abuse completed self-stigmatization, psychosis, and addiction severity measures. Most participants reported poly-drug use (49%) followed by alcohol use (42.9%). Multiple regression analyses were employed to identify direct effects, while bootstrap mediator analyses identified indirect effects through the hypothesized mediators.
Results: The findings suggested that psychosis severity was related to low self-esteem, but not low self-efficacy. Addiction severity was also related to changes in self-esteem. Stereotype concurrence was found to mediate the relationship between psychosis severity and self-esteem, as well as, self-efficacy.
Conclusions: Self-stigma has been linked to reductions in self-esteem and self-efficacy in individuals diagnosed with schizophrenia, as well as, individuals diagnosed with a substance use disorder. Self-stigmatization has further been linked to poor treatment compliance and relapses in individuals meeting criteria for schizophrenia, as well as, a substance use disorder, thus impeding recovery and promulgating stigmatizing beliefs. While researchers have addressed the role of self-stigma in each of these populations separately, the role of self-stigma in individuals with co-occurring schizophrenia and addiction has not been adequately addressed. Treatment implications are discussed.
Financial Support: None.

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TWELVE MONTHS OF NIGHTLY ZOLPIDEM DOES NOT PRODUCE WITHDRAWAL SYMPTOMS ON DRUG DISCONTINUATION: A PROSPECTIVE PLACEBO-CONTROLLED STUDY.

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Aims: Animal studies have demonstrated physical dependence with benzodiazepine receptor agonists (BzRAs). In patients chronic use of therapeutic doses of BzRA anxiolytics is associated with withdrawal, but reports of withdrawal with BZRA hypnotics are less conclusive. This study prospectively tested for withdrawal symptoms after 12 months of nightly use of the BzRA hypnotic,zolpidem 10mg.
Methods: 29 DSM-IVR defined primary insomniacs, ages 32-64 yrs, with a sleep efficiency (sleep time/bed time) of <85% and no other primary sleep disorders on a 8-hr sleep recording, without psychiatric disorders, drug dependency and in good general health participated. Participants received 10 mg zolpidem or placebo, double-blind, nightly for 12 months. Weekly information regarding medication compliance and sleep was collected via IVRS. On two laboratory nights in Months 1, 4, and 12, placebo was administered to both groups and the Tyrer Benzodiazepine Withdrawal Symptom Questionnaire (a 20 symptom rating scale,0-2) was completed in the morning.
Results: On the IVRS participants reported taking 73-89% of nightly capsules and the groups did not differ (placebo: 81+0.04% vs zolpidem: 84+0.03%). At month 12 the total Tyrer score (mean night 1 and 2 of discontinuation) did not differ between the placebo and zolpidem groups: 1.2+1.7 vs 1.6+1.7 (a score >20 is considered clinically significant). The number of severe symptom ratings (2) given for any one of the 20 symptoms was 3/15 in the placebo group and 1/14 in the zolpidem group. Placebo and zolpidem groups did not differ in their ratings on any of the 20 symptoms individually.
Conclusions: In insomniacs, zolpidem 10 mg was not associated with withdrawal after chronic nightly administration, suggesting with hypnotics, a condition in which receptors are unoccupied for 16 hours a day, there is no withdrawal. This contrasts with BzRA anxiolytics, where receptors are occupied all day, and withdrawal is reported.
Financial Support: NIDA, grant#: R01DA17355 awarded to Dr. Roehrs

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DECREASING STIGMATIZING ATTITUDES ABOUT SUBSTANCE ABUSE AMONG UNIVERSITY UNDERGRADUATE CRIMINAL JUSTICE STUDENTS: IMPLICATIONS FOR PREPARING FUTURE PROFESSIONALS.

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Aims: To examine undergraduate criminal justice (CJ) students' stigmatizing attitudes about addiction and individuals who have substance use disorders (SUDs).
Methods: The study was conducted over a two-year period with University of Nevada, Reno CJ introductory courses using a non-equivalent control group design and mixed method pre/post-test attitude measures. As part of their regular course instruction, the implementation group received three hours of neuroscience of addiction lecture and educational activities with a CJ enhancement (e.g., NIDA Principles of Treatment for CJ, 2006).
Results: A total of 272 students completed pre/post-test surveys: Implementation group (n = 90); Control group (n = 182). Results showed a significant decrease in stigmatizing attitudes following the Curriculum infusion between implementation vs. non-implementation groups and implementation group pre-test vs. post-test measures (qualitative and quantitative item level analyses will be presented).
Conclusions: Currently, over half of all individuals incarcerated meet the criteria for SUDs (Mumola & Karlberg, 2006). As such, it is important that CJ professionals understand the neurobiological basis for addiction as the shift in knowledge and attitudes could positively impact current sanction-based system approaches (Chandler, Fletcher, & Volkow, 2009). Results lend support to the effectiveness of infusing a brief research-based neuroscience of addiction Curriculum into existing undergraduate CJ courses on significantly reducing stigmatizing attitudes related to addiction and individuals with SUDs. Preparing CJ students to identify and treat substance abusing offenders will increase their effectiveness as professionals, while having potentially long-term implications regarding public health and safety issues.
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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INTRANASAL ABUSE POTENTIAL OF IMMEDIATE-RELEASE OXYCODONE (ACUROX®; IROA) FORMULATED TO DETER ABUSE.

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Aims: IRO-A is an orally administered, immediate-release tablet of oxycodone HCI with functional excipients intended to impede intranasal and intravenous abuse. We compared the abuse potential of crushed IRO-A tablets with crushed commercially available immediate release oxycodone HCI (IRO) tablets when administered intranasally to nondependent recreational opioid users.
Methods: This was a single-center, single-dose, randomized, double-blind, active-controlled, 2-way crossover study. Nondependent, recreational opioid users (confirmed by naloxone challenge) who were experienced with intranasal opioid administration self-administered 2 crushed IRO-A (15 mg) or 3 crushed IRO (15 mg) tablets intranasally on separate days. Primary endpoints assessed with bipolar visual analogue scales (VAS) were maximum effect (E_{max}) for Drug Liking, and effects at 8 hours postdose for Take Drug Again and Overall Drug Liking. The VAS scores were analyzed using a linear mixed model. Secondary endpoints included pupillometry, nasal effects, and safety assessments.
Results: Forty subjects received at least 1 drug dose (safety population); 39 subjects were evaluable (1 subject was excluded for vomiting). Subjects were 35.7±10.2 (mean±SD) years old, mostly male (80%), and white (75%). Compared with IRO, crushed IRO-A was associated with significantly lower least squares mean VAS scores for Drug Liking E_{max} (93.5 vs 70.8; 3.3 (SE); P<0.0001), Take Drug Again E_{8h} (91.3 vs 45.9; 5.2 (SE); P<0.0001), and Overall Drug Liking E_{8h} (87.4 vs 47.8; 4.4 (SE); P<0.0001). Pupillary response was similar for both treatments. Euphoric mood, somnolence, and pruritus adverse reactions were more common with IRO. Nasal effects (e.g.: rhinorrhea, nasal congestion, and nasal discomfort) were more common with IRO-A.
Conclusions: Crushed intranasal IRO-A has lower abuse potential than crushed IRO due to functional excipients in IRO-A.
Financial Support: Supported by King Pharmaceuticals, Inc.

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CAN CLINICAL TRIAL ADVERSE EVENTS PREDICT PHARMACOLOGICAL RESPONSE?

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Aims: To make a preliminary exploration of relationships between subject-reported adverse events (AEs) and direct pharmacodynamic measures in human abuse potential studies. Although used to evaluate abuse potential, the association between clinical trial AEs and direct pharmacodynamic measures has not been elucidated.
Methods: AE data from comparators in single-dose, randomized, double-blind crossover abuse potential studies were coded using MedDRA and compared with pharmacodynamic results. AEs were categorized as 'core' terms (actual abuse/dependence [AD]) and those suggestive of mood-elevating (ME), sedative (SED), stimulant (STI), perceptual (PER) or cognitive/motor impairment (CMI) effects and summarized by drug/class (% incidence).
Results: AD reports were very rare; only 1 AE was reported in >1000 exposures, even with known drugs of abuse in recreational drug users. The highest incidence of ME events (eg, euphoric mood) was observed with opioids, ketamine and cannabinoids (≥50%), and stimulants (~30-40%). Sedative-hypnotics were associated with the lowest incidence of ME events (<30%) among drugs of abuse. AE patterns were generally consistent with pharmacodynamic results. Compared with placebo, stimulants had a higher incidence of ME and STI AEs, while SED incidence was lower than placebo, and CMI AEs were rare. Ketamine, opioids and cannabinoids were associated primarily with ME events, with SED events observed in the latter 2 classes. PER events were higher with cannabinoids/ketamine than placebo but lower compared to other types of events. Sedative-hypnotics were associated primarily with SED events (>90% at some doses), with a lower incidence of ME, PER and CMI events. Overall AE patterns were generally consistent across studies; however, absolute incidence was variable for some AEs (even with identical doses of a given drug), suggesting that non-drug factors may influence reporting.
Conclusions: This preliminary evaluation indicated that AEs were generally consistent with pharmacodynamic results suggesting that clinical trial AE patterns may be useful for signaling pharmacologic response.
Financial Support: Kendle

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RANDOMIZED CONTROLLED TRIAL OF A WEB-BASED INTERVENTION FOR CANNABIS USE.

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Aims: This study aims to test the efficacy of "Reduce Your Use", a new web-based treatment for cannabis use. The treatment employs CBT and MI strategies. Its six core modules are: Feedback and Building Motivation; Managing Smoking Urges and Withdrawal; Changing Your Thinking; Coping Strategies and Skill Enhancement; Activities and Interpersonal Skills; and Relapse Prevention. It is hypothesised that cannabis users who receive the treatment will show larger reductions in cannabis use and dependence symptoms than will cannabis users who receive a placebo control treatment.
Methods: Two hundred individuals who want to quit or reduce their cannabis use will be recruited for the study. So far, 158 participants have been enrolled and randomly assigned to receive either the web-based intervention, or a placebo control treatment consisting of 6 modules of online educational information.
Results: Six weeks post-intervention results are currently available for 81 participants, while 3-month follow-up results are available for 59 participants. Follow-up data showed significantly larger reductions in cannabis dependence symptoms (measured using the Severity of Dependence Scale) in the intervention group relative to the control group, with a mean change score difference of 2.48, p = .04. Additionally, past-month abstinence was significantly higher in the experimental group compared to the control group (44% versus 17% of available cases, p = .03). Reductions in past-month cannabis use were greater in the experimental group by an average of 2.65 days and 4.64 standard cannabis units. These differences did not reach significance with the current N of 59.
Conclusions: Initial results suggest that Reduce Your Use may be an efficacious treatment for individuals who want to quit or reduce their cannabis use.
Financial Support: This research was funded by the Department of Health and Ageing, Australia.

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A COMPARATIVE STUDY OF SUGAR, MARIJUANA, COCAINE AND ALCOHOL DEPENDENCE: A CONSTRUCT ANALYSIS USING ITEM RESPONSE THEORY.

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Aims: Item Response Theory (IRT) models are statistical tools that evaluate the psychometric properties of instruments by organizing their items or components according to a hierarchical order of different levels of severity of the measurable construct. The aim of this study was to examine the psychometric properties of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the diagnostic criteria for sugar, marijuana, cocaine and alcohol dependence using the IRT method.
Methods: In this study, a convenience sample of 803 individuals (48% female, mean age 34±12yrs, 100% sugar users, 23% marijuana users, 16% cocaine users, 66% alcohol users) responded to a questionnaire on sugar and other psychoactive substance dependence based on DSM-IV criteria for substance dependence. Data were collected in two Brazilian state capitals and analyzed by the Item Response Theory.
Results: DSM-IV criterion symptoms of sugar, marijuana, cocaine and alcohol dependences indicated a good reliability (cronbach alpha coefficient ≥0.78). The IRT results showed for each substance the severity levels of dependence for each DSM-IV criteria (sugar: -2.9 – 3.6; alcohol: -1.4 – 2.0; cocaine: -0.8 – 1.4; marijuana: -1.0 – 1.5). The less severe symptom for sugar was "taking large amounts", for alcohol and cocaine "taking large amounts" and "continued use despite having problems" were the less severe symptoms and for marijuana was "continued use despite having problems". The most severe symptoms for sugar and alcohol were "giving up important activities" and for cocaine and marijuana were "unable to cut down".
Conclusions: These results are important to reinforce a hypothesis of sugar dependence using the DSM-IV criteria and other addictive substances. Data also show that sugar and other psychoactive substance present similarities between DSM-IV dependence criteria and level of severity.
Financial Support: CNPq; FAPEMIG

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PHOTOVOICE AS A WAY TO ENGAGE AND RETAIN OLDER AFRICAN-AMERICAN METHADONE CLIENTS.

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Aims: Using the innovative technique of photovoice - a participatory means of sharing knowledge and expertise through visual images and accompanying narratives - this study provides some of the first data on older adult African American methadone clients from their perspective.
Methods: In photovoice, people receive cameras, which allow them to act as recorders and potential catalysts for change in their communities. University researchers collaborated with ten African American methadone clients (5 men, 5 women) over age 50, meeting for six weekly 2-hour sessions. Participants chose a weekly theme and in the ensuing week took pictures related to that topic. Photographs from the previous week were brought to the next session, during which participants engaged in individual and group discussions. The analysis process was also collaborative; participants and university researchers met for three additional sessions to identify commonalities and differences among the photographs and to select and arrange photographs and narratives for public presentation.
Results: Participants documented their motivation for deciding to enter treatment, the barriers to accessing and remaining in treatment as an older adult, and the desire to be successful in treatment. Extensive caregiving responsibilities for grandchildren and other family members, although burdensome, provided motivation for drug abstention.
Conclusions: The photographs and accompanying narratives are particularly useful for policy and practice changes. Training of staff, understanding of physical limitations, and transportation assistance will be necessary requirements for successful engagement and retention of older adult clients.
Financial Support: Staunton Farm Foundation

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SUICIDALITY AND CONTINUED OPIOID MISUSE IN METHADONE PATIENTS: THE ROLE OF MINDFULNESS AND EXPERIENTIAL AVOIDANCE.

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Aims: Suicidal thoughts and behaviors are common among individuals with substance use disorders (SUDs). Evidence suggests suicidality is associated with SUD treatment outcomes. Mindfulness and experiential avoidance are associated with suicidality. This study examines whether these two constructs mediate the association between suicidality and continued opioid misuse in patients enrolled in methadone maintenance therapy (MMT).
Methods: We surveyed 100 individuals enrolled in MMT with co-occurring chronic pain. Substance use was assessed by Time Line Follow Back method. The MINI International Neuropsychiatric Interview assessed suicidality. To measure mindfulness and experiential avoidance, we used the Mindfulness Attention Awareness Scale (MAAS) and the Acceptance & Action Questionnaire (AAQ).
Results: Participants were 51% female, mean age was 40 years old (SD 11). Overall, 67% reported current suicidality (at least one suicidal thought) in the past month. Overall, 54% of respondents reported opioid misuse at least once in the past month. Suicidality was significantly correlated with mindfulness($r=-.32$, $p\leq.01$), experiential avoidance($r=-.35$, $p\leq.01$), and opioid misuse($r=.30$, $p\leq.01$). We examined mindfulness and experiential avoidance as mediators of the association between suicidality and continued opioid misuse. No significant mediation effect was observed for experiential avoidance. However, mindfulness significantly mediated the relationship between suicidality and chronic pain (Sobel $Z=2$, $p\leq.05$; bootstrapped point estimate=.26; 95%CI .0695-1.0780) indicating complete mediation of the association between suicidality and misuse.
Conclusions: Mindfulness-based interventions are gaining increased attention as effective approaches to address myriad psychological disorders including SUDs and suicidality. This study provides further support for the importance of mindfulness in continued opioid misuse. Results from this study may have implications for how to best address the treatment needs of this clinical population.
Financial Support: DA022297(Potter)

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HEROIN USE IS A RISK FACTOR FOR INJECTING PRESCRIPTION OPIOIDS.

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Aims: To describe the prevalence and correlates of prescription opioid (PO) injection among patients enrolling in opioid treatment programs (OTPs).
Methods: Enrollees in 5 OTPs who were abusing POs completed a survey regarding non-medical opioid use and injection. Demographics and opioids used in the past month were entered (stepwise) in a logistic regression model to predict injection of POs. Significance was $p < .05$.
Results: Among the 752 OTP enrollees, 423 (56%) reported using POs during the past month. Among these PO users mean age was 35, 56% were male; race/ethnicity was 73% White, 8% Black, 14% Latino. The most frequently abused POs were oxycodone (56%), hydrocodone (48%), and methadone (36%); 61% had used heroin in the past month. More than half (54%) reported injecting any opioid in the past month; 45% injected heroin, 37% injected POs. Among PO users who also used heroin, 78% (200/257) reported injecting any opioid and 51% (130/257) reported injecting POs. The past month injection rate among enrollees who did not use heroin in the past month was 16% (27/166) and 10% (8/84) among those who had never used heroin. The univariate relationship between past month heroin and past month PO injection was OR=5.30 (CI: 3.29 to 8.57). In the multivariate model, opioids used in the past month that significantly predicted PO injection were heroin (OR=5.61), hydrocodone (OR=.637), and fentanyl (OR=2.18). Black ethnicity also predicted PO injection (OR=2.24). When a covariate representing PO as a primary drug was forced entered into this model, heroin use (either lifetime or past 30 days) remained a significant predictor of PO injection. In a separate model, current and lifetime heroin use were simultaneously entered as covariates and each was significantly associated with PO injection.
Conclusions: Current and past heroin use is strongly associated with injection of POs even among opioid dependent patients who identify a PO as their primary drug. Targeted HIV/HCV screening and prevention protocols may be needed for PO abusers with a heroin use history.
Financial Support: Denver Health is part of the Researched Abuse Diversion and Addiction-Related Surveillance(RADARS®)System.

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IDENTIFICATION OF "PARTIAL" SUBSTRATES FOR THE BIOGENIC AMINE TRANSPORTERS.

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Aims: Drugs that interact with the biogenic amine transporters (BATs) can be broadly categorized as either uptake inhibitors or releasers. In the course of evaluating compounds from a phenethylamine library (PAL) as NET, DAT and SERT-releasers, we identified several PAL-compounds that appeared to be partial substrates. The aim of this study was to characterize these compounds in greater detail. We tested the hypothesis these compounds display partial release characteristics in the in vitro assay because they induce efflux of neurotransmitter at a slower rate than full substrates.
Methods: BAT-release assays used rat brain synaptosomes and followed published procedures. [3H]MPP+ was used to assess release from DA- and NE-nerves terminals, while [3H]5-HT was used to assess release from 5-HT nerve terminals. DAT-efflux assays were conducted by following the efflux of [3H]MPP+ following the addition of test compounds.
Results: Several compounds were partial DAT substrates: PAL-192 (EC50=622 nM, Emax=61%), PAL-193 (EC50=507 nM, Emax=65%). Other compounds were partial SERT substrates: PAL-1045 (EC50=12 nM, Emax=66%), PAL-153 (EC50=561 nM, Emax=54%); others were partial NET substrates: PAL-218 (EC50=56 nM, Emax=62%), PAL-874 (EC50=305 nM, Emax=75%). In the DAT efflux experiments, full substrates like D-AMPH promoted a fast efflux component (K1 =0.24 min-1) and a slow efflux component (K2=0.008 min-1). For the partial DAT substrates, K1= ~0.04 min-1 and K2 approximated 0.
Conclusions: Partial DAT substrates promote efflux at a slower rate than full substrates. The "partiality" of the release curves reflects the ultra-slow K2 constant. We speculate that partial BAT substrates bind to the transporter but are less effective in inducing the conformational changes required for substrate transport.
Financial Support: Supported by the IRP, NIDA, NIH, DHHS and NIDA Grant R01 DA12970 to Dr. Blough.

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IMPACT OF INPATIENT RESEARCH PARTICIPATION ON SUBSEQUENT HEROIN USE PATTERNS.

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Aims: Research on drug dependence often involves the administration of drugs of abuse to experienced drug users under controlled laboratory conditions. Although these experimental studies have improved our understanding of drug dependence, questions remain about the impact of drug exposure in the laboratory on subsequent drug use patterns of the participants. The objective of the present study was to assess the extent to which participation in an experimental study altered the frequency of heroin use after study completion.
Methods: Data were collected from 4 studies based on laboratory sessions involving opioid administration that took place in the Substance Use Research Center of the New York State Psychiatric Institute. Participants' self-reported heroin use, measured in terms of dollars spent per day prior to and one month after study participation, was compared with Wilcoxon signed-rank tests.
Results: Of the 66 heroin users enrolled in the 4 studies, the mean age was 37.7 +/- 4.9 (25-46) years and 86.4% were men. They reported using less heroin one month after study participation. Specifically, the amount of money spent on heroin decreased from $65/day at baseline to $16/day one month after study completion. Statistical analyses revealed that the decrease in heroin use was significant ($p<0.001$).
Conclusions: These findings demonstrate that participation in opioid administration studies does not increase subsequent opioid use. The amount spent on heroin decreased one month after study participation, which is a key indicator of degree of drug use. Further research is required to better understand the relationship between completion of experimental studies and subsequent drug use patterns.
Financial Support: Supported by DA09236, as well as investigator-initiated grants from Schering-Plough and Grunenthal USA.

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BRIEF TRAUMA AND MENTAL HEALTH ASSESSMENTS FOR FEMALE OFFENDERS IN ADDICTION TREATMENT.

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Aims: Increasing numbers of women in prison raise concerns about gender-specific problems and needs severity. Female offenders report higher trauma as well as mental and medical health issues than males, but large inmate populations and limited resources create challenges in administering proper diagnostic screening and assessments. This study focuses on brief and flexible 1-page forms that address specialized trauma and health problems, along with related psychosocial functioning.
Methods: Women from two prison-based treatment programs for substance abuse were assessed (N=1397), including one facility for "special needs" and one for "regular" female offenders. Assessments included the TCU Trauma form (17 symptom-severity items representing post-traumatic stress disorder) and the TCU Health form (11 items about types of physical disease or health problems experienced in the past year, and 10 items on symptoms of psychological distress during the past 30 days).
Results: As expected, females in the special needs facility reported more posttraumatic stress symptoms, higher rates of psychological stress and previous hospitalizations, and more health issues at admission. Both mental health and trauma assessments were highly correlated with independent psychological functioning assessments including, higher anxiety and depression, lower self esteem, and lower decision making scores. Offender's social functioning relationships were also consistent. Higher levels of psychological stress were related to greater hostility, more risk taking, and lower social support levels.
Conclusions: Findings support use of these forms to identify needs and functioning of female offenders, and their applications as tools for monitoring progress and change over time are discussed.
Financial Support: Funding was provided by the National Institute on Drug Abuse, National Institutes of Health (NIDA/NIH)through grants to Texas Christian University R37DA13093 and R01DA025885.

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EATING BEHAVIORS AND RELAPSE AMONG PHYSICIANS RECOVERING FROM SUBSTANCE USE DISORDERS.

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Aims: To explore the relation between changes in substance use and eating behavior among physicians with a substance use disorder history.
Methods: We surveyed 80 physicians (85.1% male and 90.9% Caucasian) who participated in the Florida Physician Health Program between 1994-2008. Participants completed an anonymous online survey. Items assessed substance use, recovery status, relapse history, and weight change. The Eating Behaviors Questionnaire (EBQ) was used to measure food addiction symptoms.
Results: The majority of physicians gained weight after achieving sobriety, but most (92.5%) denied significant symptoms of food addiction (EBQ M = 2.03, SD = 0.62). There was significant variability in weight change, with 10.1% gaining >30 lbs and 2.9% losing >30 lbs. Although the relation between weight change and relapse was not statistically significant ($X^2 = 7.51$, $p = .11$), clinically-significant differences were noted. All physicians who lost >15 lbs avoided relapse to substance use, but 26.8% of those whose weight change was < 15 lbs relapsed, and 43.5% of those who gained >15 lbs relapsed. There were no significant differences in food addiction between physicians who relapsed and those who did not. Participants with a history of depression or eating disorder reported more severe food addiction symptoms ($t = 2.44$, $p = .02$ and $t = 3.48$, $p = .001$, respectively). T-tests comparing smokers and non-smokers on measures of weight change and food addiction showed no significant differences.
Conclusions: The majority of physicians recovering from substance use disorders denied feeling addicted to food, which suggests that most physicians do not experience a "transfer" of addictive behaviors from drugs to food. Weight gain did not appear to protect against relapse; whereas weight loss was associated with improved outcome. Future research should examine whether efforts to promote healthy lifestyles may assist recovering physicians in maintaining sobriety.
Financial Support: Professionals Resource Network, Inc., an integral arm of the Florida Medical Association.

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SCREENING FOR CO-OCCURRING MENTAL DISORDERS: FROM RESEARCH VALIDATION TO KNOWLEDGE TRANSLATION.

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Aims: We aimed to engage treatment providers in the process of selecting and validating screening tools and then field testing a clinical protocol.
Methods: A 'roadmap' was developed that mapped clinical issues and potential tools to three phases of the treatment process: screening, assessment and treatment planning. An international symposium was then organized to clarify research and practice priorities. A study then compared the accuracy of four screening tools for the identification of mental disorders in 545 clients with substance use problems using the SCID diagnostic interview as the gold standard and ROC analysis. A second project tested the feasibility of implementing a two-staged approach to screening in three treatment services.
Results: Although the GAIN-Short Screener; K6; Psychiatric Sub-scale of the Addiction Severity Index; and Psychiatric Diagnostic Screening Questionnaire (PDSQ) all performed in the good to very good range (e.g., AUC for any past-month disorder ranged from 0.82 (PDSQ) to 0.77 (ASI Psychiatric Subscale), the GAIN-SS was marginally more efficient. For specific disorders the PDSQ was the most accurate suggesting potential value of a two-staged screening process using the GAIN-SS for case-finding and the PDSQ for case-defining. The field testing of the two-stage protocol showed that while staff and clients perceived the utility of both the tools each agency was unique in the benefits and challenges identified.
Conclusions: While the data support the use of any of the evaluated screening tools among clients presenting for substance use treatment the GAIN Short Screener is of particularly high value given its accuracy as well as flexibility, low cost and ease of administration. Results of the knowledge translation component highlight the need to take into account local context and to be adaptable to the unique intake and assessment processes within each organization.
Financial Support: This project was supported by a research award from the Canadian Institutes for Health Research: Grant #119685

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D-AMPHETAMINE AND ATOMOXETINE FOR METHAMPHETAMINE ABUSE.

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Aims: Behavioral therapies reduce methamphetamine use, but many patients are unable to achieve long periods of abstinence suggesting other strategies like pharmacotherapy are needed. These experiments determined the subjective and physiological effects of intranasal methamphetamine in non-treatment seeking stimulant-dependent participants maintained on d-amphetamine, a dopamine releaser, and atomoxetine, a norepinephrine transport inhibitor. d-Amphetamine maintenance attenuated the behavioral effects of cocaine in previous studies, so we predicted d-amphetamine maintenance would attenuate the subjective effects of methamphetamine. Acute atomoxetine pretreatment attenuated the behavioral effects of d-amphetamine in a previous study, so we predicted atomoxetine maintenance would also attenuate the subjective effects of methamphetamine. We also predicted methamphetamine would be well tolerated during d-amphetamine and atomoxetine maintenance.
Methods: Two separate experiments were conducted. Two maintenance conditions were completed in counterbalanced order in each experiment (0 and 45 mg/day d-amphetamine [Exp. 1; N=8]; 0 and 80 mg/day atomoxetine [Exp. 2; N=6]). After at least 7 days of maintenance, participants were administered ascending doses of intranasal methamphetamine across two experimental sessions (0, 2.5, 5, 10 and 20 mg [Exp. 1]; 0, 5, 10, 20 and 30 mg [Exp. 2]). Methamphetamine doses were separated by 90 minutes. Repeated measure ANOVA was used to analyze the data.
Results: During placebo maintenance methamphetamine produced prototypical behavioral (e.g., increased ratings of Like Drug) and physiological effects (e.g., increased blood pressure) in both experiments. d-Amphetamine maintenance attenuated some of the subjective and physiological effects of methamphetamine, while atomoxetine maintenance did not. Two more participants will be enrolled in Exp. 2.
Conclusions: These results are concordant with those of previous studies with cocaine and suggest agonist therapies like d-amphetamine may be a viable strategy for managing methamphetamine dependence.
Financial Support: Supported by NIDA R01 DA025032.

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DETERMINING THE EFFECTS OF AN ACUTE DOSE OF TRIFLUROMETHYLPHENYLPIPERAZINE ON THE HUMAN REWARD PATHWAY USING A GAMBLING TASK.

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Aims: TFMPP is a non- selective serotonin (5HT) agonist, and a common constituent in a group of designer drugs. Literature has indicated that 5HT influences reward modulation, especially in the nucleus accumbens and affects dopamine transmission via the 5HT2C receptor. TFMPP's stimulus properties appear to be modulated via 5HT1B and 5HT2C receptors. This study is a randomised double blinded cross-over trial to determine the effects of TFMPP on the reward pathways in comparison to placebo using functional magnetic resonance imaging (fMRI) and a gambling task.
Methods: 11 healthy subjects aged 18-40 years were imaged using fMRI (Siemens Magnetom Avanto 1.5T) and a gambling task. Echo-planar images were collected 90mins following an oral dose of TFMPP (50mg) or placebo. Subjects were tested under both drug conditions on separate occasions. Data analysis and identification of regional activation was done in SPM8.
Results: TFMPP and placebo caused changes in activation ($p<0.05$ FWE) in distinctly different areas for the conditions analyzed. TFMPP caused activation (Win$4reward - nochange$4 reward) in the right precentral gyrus Brodmann area (BA) 6 compared to placebo, whereas, placebo activated areas including the cingulate gyrus (Lose reward minus nochange reward).
Conclusions: This study is the first to investigate the effect of TFMPP on the reward pathways using fMRI. Recent studies have found the Cingulate Cortex (CC) to be activated in incentive processing. It has been suggested that the CC activates when participants are faced with risk, when behavioural errors are more likely. Our results suggest that the change in activation observed after administration of TFMPP may be due to less thought about the consequences of risky behavior.
Financial Support: School of Pharmacy, The University of Auckland

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BRAIN ACTIVITY RELATED TO DECISION-MAKING AMONG ADOLESCENTS IN SUBSTANCE ABUSE TREATMENT.

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Aims: Performance on delay discounting (DD) tasks is hypothesized to reflect activity of the neural systems involved in addiction. The current study examined this hypothesis using functional neuroimaging with adolescents who abuse substances.
Methods: Adolescents being treated for substance abuse or dependence completed a DD task that was optimized for functional neuroimaging in a Philips Achieva 3.0 Telsa X-Series MRI scanner. Neural activation associated with making preference decisions about hypothetical monetary rewards across several delays was compared to activation in control 'no-choice' trials. In addition, a pre-scan DD task with the same delayed reward magnitude ($1000) was completed prior to the fMRI session (*M* days =15.86; *SD* =8.17). DD rate (log*k* value) from this task was tested as a predictor of neural activity while making DD decisions in the scanner (i.e., choosing smaller amounts now or choosing $1000 later versus control 'no-choice' decisions). Image preprocessing and statistical analyses were performed using AFNI software.
Results: Fourteen adolescents (*M* age = 15.57; *SD* =1.50) met DSM-IV criteria for marijuana or alcohol abuse or dependence. All neuroimaging results met a p-value threshold of less than 0.005 and a cluster size of at least 20 voxels (3 mm^3). Results revealed that decision making engaged the bilateral inferior frontal gyri, dorsal anterior cingulate cortex, right anterior insula, and bilateral superior parietal lobules. Results also indicated that pre-scan DD values were linearly related to activation in the subgenual cingulate while making DD decisions in the scanner.
Conclusions: Consistent with the adult addiction literature, results revealed that decision making within the scanner was related to neural circuitry involved in cognitive control. In addition, higher pre-scan DD (i.e., more impulsive decision making) was associated with neural processes that reflect increased activity in affective neural circuitry.
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COMPUTER-DELIVERED PSYCHOSOCIAL TREATMENT FOR OFFENDERS WITH SUBSTANCE USE DISORDERS.

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Aims: To test, among a sample of incarcerated offenders with substance use disorders, the comparative effectiveness of a computer-based psychosocial treatment program, the Therapeutic Education System (TES) vs. Standard Care. It is predicted that as compared to Standard Care, participants in TES will have significantly better outcomes on measures of drug use, HIV risk behavior and crime
Methods: This ongoing ARRA-funded NIDA study, begun in 2009, employs random assignment to either (1) TES, or (2) Standard Care, in a multi-site trial conducted in 4 States and 10 prisons. This prospective longitudinal study obtains follow-up data post prison discharge; interviews at 3- and 6-months and official record data of re-incarceration between 8 and 14 months.
Results: A total of 513 subjects were recruited (TES N=258; Control N=255). Subjects from both groups attended on average 50% of treatment sessions. Subjects are 71% male; 21% Hispanic, 23% Black, 52% White, and 19% American Indian. They had an extensive history of arrests (median=12); primarily abused alcohol (33%), methamphetamine (20%); crack (13%); marijuana (12%); opiates (6%); cocaine (5%); and also engaged in HIV risk behaviors during the 6 months prior to incarceration (19% injected drugs; mean of 3.94 sexual partners).
Conclusions: The study has successfully implemented a computer-delivered psychosocial treatment for offenders with substance use disorders in prison. Subjects demonstrated drug use and crime profiles typically seen in offender populations. This presentation will report 3-month post-release outcomes. The project is significant in its use of an innovative, computer-based technology and in its potential to produce a major increase in the effective and cost-effective delivery of science-based psychosocial treatment to substance-abusing offenders in prison, and thereby make a considerable public health contribution.
Financial Support: This project is supported by Award Number RC2DA028967 from the National Institute on Drug Abuse (NIDA).

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HEALTH CARE UTILIZATION AND EXPERIENCES IN PERSONS WITH SUDS: PRELIMINARY FINDINGS FROM THE HEALTH ANONYMOUS RESEARCH EVALUATION.

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Aims: Research has demonstrated people with Substance Use Disorders (SUDs) develop a diverse range of chronic health conditions. Linkages between primary care medical care and substance use treatment are of paramount importance, particularly in light of health care reform. The aim of the current anonymous health survey was to better understand health care utilization, subjective reports of health care experiences and possible barriers to medical care in persons with SUDs.
Methods: Data are derived from the Health Anonymous Research and Evaluation survey administered using an interactive program on a laptop computer at inpatient, outpatient and methadone substance use treatment centers. The HARE survey focused oncurrent rates and types of health care utilization, as well as chronic illness, mental health and current drug/alcohol use. Participants to-date are N=57 men and women who consented to the anonymous survey at one of several participating treatment programs. Final sample size expected to be N=200.
Results: Preliminary analyses found 58% of participants were male and the samples was predominantly African American (83%). Individuals reported various lengths of time in treatment including 18% less than one month and 14% reporting more than one year. The primary method of health coverage was public insurance (46%) and more than half of the sample (58%) reported having a primary care physician.
Conclusions: Further analyses of health care utilization and experiences in this representative sample of persons with SUDs will be used to guide development of care models based on patient-perceived needs and barriers. Evaluation of such models will ultimately guide development and implementation of alternative models of care compatible with the changing face of medical care and drug abuse treatment.
Financial Support: Center for Substance Abuse Treatment & U10 DA13034

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PATHWAYS TO TREATMENT: ROLE OF GENDER AND CULTURE.

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Aims: Screening and outreach services seek to expand and facilitate pathways to substance abuse treatment. One prominent pathway to treatment is criminal justice involvement. At the national level, it was the primary referral source in 37.7% of admissions in 2008. This overall figure, however, masked profound ethnic and gender differences and may underestimate criminal justice as a contributing pathway. This study examines ethnic and gender differences in pathways to treatment with the working hypothesis that men and immigrant populations would be more likely to have criminal justice involvement than women and other racial groups.
Methods: Two research assistants masked to race/ethnicity and gender categorized recorded chief complaints of all persons seeking substance abuse treatment in one region of Michigan for fiscal years 2005-06. Chief complaints were recorded using the words of the applicants. They were coded in multiple categories; no effort was made to determine primary referral source. Criminal justice category was coded if the person mentioned any criminal justice entity in their complaint.
Results: For the 7,488 admissions, 22.9% were categorized as having criminal justice involvement. In a model predicting criminal justice involvement, gender and immigrant ethnicity were both significant. Across the different racial/ethnic groups, Arab Americans had the highest rate (43.2%) followed by Latinos (37.0%). Women had overall lower rate (17.8%) than men (26.6%). For female racial/ethnic groups, Arab-American women had the highest rate (33.3%) followed by Latinas (25.5%).
Conclusions: Criminal justice involvement is a potent pathway to treatment, especially in groups that may have cultural barriers to seeking treatment. Efforts should be expanded to improve outreach services as a way to promote other pathways to treatment.
Financial Support: Supported by a grant and program support from Southeast Michigan Community Alliance.

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IMPLEMENTING DRUG SCREENING IN PRIMARY CARE: NOT FINDING WHAT WE ARE LOOKING FOR?

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Aims: One premise underlying screening and brief intervention (SBI) for drug use is that screening will identify risky use of a range of substances prior to the development of dependence. Our aim was to characterize the range and severity of drug use identified by screening in primary care.
Methods: We prospectively identified – by screening, using the ASSIST – 1,050 people in a large urban primary care practice with past 3-month drug use (ASSIST drug specific score of >=2). We enrolled 401 who completed the Composite International Diagnostic Interview-Short Form (CIDI-SF).
Results: Of 366 with a drug specific score of >=4 (the accepted cutoff for eligibility for BI), 19.9% had scores of >=27, consistent with drug dependence, while 49.7% met criteria for drug dependence based on the CIDI-SF. Of those with scores in the range of 4-26, for which BI is thought to be most appropriate, 38.6% had dependence according to the CIDI-SF. Drug of greatest concern was marijuana for 61.5%, cocaine 19.9%, opioids 16.7% and sedatives 1.9%. Drug of greatest concern included illicit use of a prescription drug for 12.8% overall.
Conclusions: Although efficacy of BI is as yet unknown, when clinicians implement drug screening in primary care settings with the belief that they will prevent more severe consequences, they may instead find nearly half of patients identified have dependence, a group not generally thought to respond to brief intervention alone. Furthermore, brief tools used to assess severity in these settings appear to yield disparate results. Finally, in primary care settings, SBI for drugs seems less likely to be a major solution for opioid, cocaine and prescription drug abuse both because of severity and because most patients identified in primary care will have marijuana use instead.
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LENGTH OF TREATMENT IS ASSOCIATED WITH DECREASE IN TOBACCO USE IN COMORBID MAJOR DEPRESSION AND ALCOHOLISM.

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Aims: Tobacco use is highly prevalent in comorbid major depression (MD) and alcoholism (AD). Few studies have examined gender differences in frequency of smoking in this population and whether treatment for depression and alcoholism has an independent impact on smoking. We hypothesized that there may be gender difference in cigarette smoking among these patients and that maximized treatment for depression and alcoholism may also impact on frequency of cigarette smoking.
Methods: We examined study hypotheses in a sample of 80 subjects (46% females) with DSM-IV/ PRISM comorbid diagnoses of MD and AD who completed a clinical trial evaluating the efficacy of fluoxetine (dose range 20–60 mg/day) +/- naltrexone (dose 50 mg/day). Patients were assessed weekly for 24 weeks with questionnaires including the Timeline Followback for alcohol and for tobacco use, and the Fagerstrom Test for Nicotine Dependence (FTND).
Results: The frequency of smoking was higher among men (61%) compared to women (39%). The mixed model with restricted maximum likelihood procedure and unrestricted covariance matrix was used. We examined whether treatment group, gender, and duration in treatment predict cigarette smoking. The results of this study showed that time in treatment was significantly associated with decrease in cigarette smoking ($p<0.01$). However there was no significant difference in the frequency of cigarette smoking between the two treatment groups or between the two genders.
Conclusions: The results of this study suggest that the length of staying in treatment may impact on the frequency of cigarette smoking regardless of gender or treatment group. While a cohort effect may explain some of these results, further studies examining factors leading to decrease in smoking among these patients are warranted.
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COMPREHENSION TESTING OF THE MEDICATION GUIDE FOR OXYCONTIN.

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Aims: Reformulated OxyContin was approved by FDA with a requirement for a REMS including a Medication Guide (MG) for patient education on the risks and safe use of OxyContin® (oxycodone HCL controlled-release) Tablets. The MG was developed by Purdue and incorporated substantial comments by FDA. This study tested patients' comprehension of the MG.
Methods: Patients using long-acting opioids, but not OxyContin (to avoid prior knowledge interfering with MG assessment), were recruited to join 1 of 3 focus group discussions (FGD) in St. Louis, Miami and New York. In Miami, participants spoke English as a second language. Participants were asked to read the MG prior to the FGD. During the FGD, they completed a questionnaire on knowledge and attitudes about the MG and OxyContin and participated in discussion.
Results: The 35 participants in the FGD answered approx. 94% of questions correctly on the questionnaire and rated the MG as easy to understand and read, appropriate length, provides useful information, and helpful for taking the drug safely. In discussion, participants stated the information was important, appreciated the thorough presentation, and appreciated that the company was "right up front" in presenting risks. Participants stated the MG could be improved by shortening, as the length would hinder reading, by removing redundant information in different sections of the MG, and consolidating information on a topic into one MG section instead of several sections. Titles and body text of sections was not clearly discerned by patients due to the use of bolded text to identify section titles and extensive use of bolding in body text to highlight important information. Patients were confused on the meaning of opiate tolerance and dependence, and how these differed from withdrawal.
Conclusions: The MG effectively communicated the most important safety messages about OxyContin; however, ways to improve the MG as a communication tool for patients were identified.
Financial Support: Supported by Purdue Pharma LP.

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CORTISOL SECRETION PROFILE AND TREATMENT OUTCOMES IN A TRIAL OF MIRTAZAPINE FOR DEPRESSED COCAINE-DEPENDENT PATIENTS.

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Aims: Dysregulated stress has been proposed as a marker of severe cocaine dependence, largely because of baseline data predicting worse treatment outcomes. Little data exists examining how treatment affects stress parameters and how these may relate to treatment outcome. In this study, we characterized diurnal cortisol secretion profiles at baseline and at end-of-study to seek if these could correlate to mood and cocaine outcomes.
Methods: This study occurred during a randomized, double-blind, placebo-controlled trial of mirtazapine (60 mg vs. pbo) for depressed cocaine dependent patients. The trial begins with a one-week lead-in, during which saliva cortisol samples are collected on day 2 and 3, at 9am, 2pm, and 5pm. At the end of the lead-in, patients are randomized, and begin an 8-week outpatient phase. Saliva cortisol is collected again at week-8. 28 patients participated. Cortisol secretion reaches its maximum in the mid-morning and gradually declines toward a nadir in the evening hours. Secretion profiles matching this were deemed TYPICAL. Any deviation from this pattern was deemed ATYPICAL. AT week 8, patient were mood responders if their HamD score decreased by >50%, and cocaine responders if use decreased by >75% from baseline. This trial is ongoing.
Results: A $\chi 2$ analysis reveals a trend: 89%(16)of patients with TYPICAL cortisol profiles were mood responders vs. 60%(9)for those with ATYPICAL profiles throughout the study, $\chi 2(1)= 3.187$, $P=.074$. No significant difference was found between groups regarding cocaine use outcome.
Conclusions: These preliminary results suggest that in depressed cocaine patients, dysregulated stress may impact mood response. Cocaine responder status did not correlate with diurnal cortisol profile at the end of treatment. Further discussion of the relationship of physiologic and subjective stress parameters to mood and cocaine outcomes (use, craving) awaits the full conclusion of this trial, and examination of unblinded medication assignment.
Financial Support: This study was supported by NIDA P50-DA09236

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DOES ALEXITHYMIA EXPLAIN VARIATION IN CUE-ELICITED CRAVING REPORTED BY DRUG-DEPENDENT INDIVIDUALS?

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Aims: Although craving is presumed to be an essential feature of the development and maintenance of drug taking behavior, several laboratory studies employing cue reactivity paradigms have documented that approximately 20-30% of addicted individuals report little or no cue-elicited craving. Given that current evidence-based treatments place a heavy emphasis on the monitoring and management of craving, it is important to understand why a significant minority of addicted persons fail to report craving. The present study examined the possibility that alexithymia, a personality attribute characterized by a difficulty identifying and describing emotions, may contribute to the impoverished cue-elicited craving experienced by some addicts.
Methods: We tested the hypothesis that alexithymia, as measured by the Toronto Alexithymia Scale (TAS; Bagby et al.1994), would be inversely related to the magnitude of cue-elicited craving obtained in a cue reactivity protocol. Forty men and women with DSM-IV Axis I methamphetamine dependence completed the TAS and provided craving ratings for methamphetamine after presentation of methamphetamine-cues. Pearson-r correlations were performed between TAS Factor scores 1, 2, and 3, measuring 'Difficulty Identifying Feelings';'Difficulty Describing Feelings'; and 'Externally-Oriented Thinking', and mean post cue craving. Independent samples t-tests compared non-cravers and cravers on mean TAS factor and total scores.
Results: Contrary to expectation, TAS factor 1 scores were positively associated with cue-elicited craving. A subset of participants (n = 13) reported no methamphetamine cue-elicited craving. No differences were found between cravers and non-cravers on TAS scores.
Conclusions: The results suggest that increasing difficulty identifying feelings may be associated with higher cue-elicited craving. Clinical implications for these findings are discussed.
Financial Support: This study was supported by NIDA Translational Research & Addictions Center, #5P20DA022658.

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BASELINE DELAY DISCOUNTING PREDICTS RESPONSE TO A BEHAVIORAL SMOKING INTERVENTION AMONG OPIOID-MAINTAINED PATIENTS.

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Aims: Delay discounting (DD) has been used in prior studies to characterize individual differences in sensitivity to reinforcement delay and, more recently, to predict treatment response in those with and without substance use disorders (Dallery & Raiff, 2007; Doran et al., 2004; Krishnan-Sarin et al., 2007; Yoon et al., 2007). DD was examined as part of two randomized trials evaluating a contingency-management intervention for reducing cigarette smoking among methadone- and buprenorphine-maintained patients (Dunn et al., 2010; ongoing study).
Methods: In both, 25 participants received a 2-week intervention wherein they received voucher-based reinforcement contingent upon biochemically-verified smoking abstinence. DD was assessed using hypothetical monetary rewards over a range of delays and examined using both the conventional k-value calculation (Mazur, 1987) and a more recently-developed ED50 calculation (Yoon & Higgins, 2008). To investigate the relationship between baseline DD and subsequent smoking abstinence, participants were dichotomized into low (Low I, n=15) and high (Hi I, n=10) impulsivity groups based on baseline ED50.
Results: Preliminary analyses show that Low I participants achieved more smoking abstinence during the intervention than Hi I (63.4% vs. 32.1% smoking-negative samples; $p < .001$, respectively). When participants were also dichotomized based on whether they abstained (n=15) or continued to smoke (n=10) during the study, Abstainers had significantly lower baseline k-values (.001 vs. .003; p=.02) and marginally higher ED50 values (2.72 vs. 0.83 years; p=.12) than Smokers, respectively.
Conclusions: These preliminary data suggest that baseline DD may be associated with subsequent response to a smoking intervention and extend these findings to opioid-maintained smokers.
Financial Support: NIDA T32 DA007242 and R01 DA019989

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PREVALENCE OF MOOD AND SUBSTANCE USE DISORDERS AMONG PATIENTS SEEKING OFFICE-BASED BUPRENORPHINE.

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Aims: Psychiatric comorbidity can adversely impact treatment of opioid dependence. While the prevalence of psychiatric comorbidity among patients in methadone maintenance treatment has been established, the extent to which these findings extend to opioid dependent individuals seeking office-based buprenorphine-naloxone treatment (BNT) is currently unclear. This study explored the prevalence of mood and substance use disorders among patients seeking BNT.
Methods: 248 consecutive patients seeking BNT were evaluated using specific modules from the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). For this study, lifetime and current diagnoses were mutually exclusive; thus, lifetime prevalence rates do not include current diagnoses and vice versa.
Results: Patients ranged in age from 18 to 62 years old (M = 34.1, SD = 10.0); 181 (73%) were men; 206 (83%) were white. Major depression was the most prevalent mood disorder among the study sample (21% current, 23% lifetime). A minority of patients met criteria for current or lifetime dysthymia (5%) or mania or hypomania (2%). While seventeen percent of patients met current criteria for abuse of or dependence on at least one non-opioid substance (7% alcohol, 7% cocaine, 4% marijuana, 2% benzodiazepines, 0.4% stimulants, 0.4% polydrug), sixty-eight percent met lifetime criteria (39% alcohol, 37% marijuana, 29% cocaine, 9% benzodiazepines, 8% hallucinogens, 4% stimulants, 1% polydrug, and 0.4% other). One patient (0.4%) did not meet criteria for current or lifetime opioid abuse or dependence.
Conclusions: The prevalence of psychiatric comorbidity in patients seeking office-based BNT is high and supports the need for clinicians to assess and address these conditions.
Financial Support: Supported by NIDA K23 DA024050, K24 DA00445, and R01 DA019511

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PUTTING DOWN THE BOTTLE: EXPLORING THE ADAPTABILITY OF SKILLS USED TO DECREASE PROBLEMATIC DRINKING AMONG HEROIN AND COCAINE USERS.

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Aims: The current study examines traits of individuals who reported ceasing problematic alcohol use without the assistance of professional drug/alcohol treatment services and discusses the potential applicability to the cessation of more deleterious substances.
Methods: A cross-sectional, retrospective study of the baseline data from the Baltimore site of the NEURO-HIV Epidemiologic Study focusing specifically on self-reported alcohol, heroin, and cocaine use.
The sample consisted of 338 participants who reported having used heroin and/or cocaine in the past six months and having had a period in their lives when they drank alcohol daily for three or more consecutive months. Active heroin and cocaine users were divided into three groups based on current levels of alcohol use and NIAAA definitions of problem drinking in the previous 30-days: abstainers, moderate alcohol users, and problematic alcohol users.
Results: In the current study, 69.3% of current heroin and/or cocaine users reported that at one time in their lives they drank alcohol on a daily basis for three or more months, but currently were no longer engaging in problematic drinking. Of those, 45.7% reported they stopped drinking entirely without any form of professional help. The current study explores executive functioning skills and protective factors of those who were able to abstain from problem drinking either by reducing their alcohol intake to moderate levels or abstaining from alcohol consumption entirely and compares them to individuals who were currently still engaging in problematic drinking behaviors.
Conclusions: The recovery process from chronic problematic alcohol use may provide strengths which could translate into recovery from heroin and/or cocaine or other deleterious substances. The authors explore the feasibility of capitalizing on these strengths in a series of interventions to promote reduction or cessation of heroin and/or cocaine use.
Financial Support: This study was supported by grants R01DA014498 and T32DA007292 from the National Institute on Drug Abuse

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LIFE STRESSORS AND SUBSTANCE USE AMONG ISRAELI ADOLESCENTS.

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Aims: Past-year stressful life events is associated with increased risk for PTSD symptoms (McLaughlin, et al., 2010). The present study,conducted one year after Israel's second Lebanon War in which civilians were almost exclusively affected, explores whether a macro stressful event occurred in the past year,i.e.,exposure to war,is associated with increase likelihood for PTSD and substance use.We hypothesize that:(a)Exposure to war events in the past 12 months will be associated with increase likelihood for PTSD controlling for background variables [gender, age, ethnicity (Jewish/Arabs)] and earlier traumatic events;(b)Exposure to war and PTSD will be associated with increase likelihood for substance use controlling for background variables and earlier traumatic events.
Methods: 1,800 Jewish and 2,351 Arab (about half were boys) 7th – 11th grade students were enrolled in a representative sample of students in northern Israel.Self report measures included (a)exposure to negative life events;(b)exposure to wartime events; (c)likely PTSD; (d) use of substances (on a 5-point scale; 1=never; 5=every day).
Results: 11.3% of female (13.8% and 7.7% of Arab and Jewish) students and 7.2% of male (9.7% and 4.8% of Arab and Jewish)students reported symptoms indicating likely PTSD. Students who were exposed to war events are 1.21 to 1.40 (for 3 types of exposure) more likely to experience PTSD controlling for background variables and negative life events. Students with PTSD related to war events are 1.44 (CI 1.08,1.91) more likely to smoke cigarettes, 1.38 (CI 1.04,1.83) more likely to consume alcohol, 3.48 (CI 2.40,5.06) more likely to use cannabis and 4.06 (CI 2.73,6.04) more likely to use ecstasy controlling for background variables and negative life events.
Conclusions: This study expands McLaughlin's findings to include current stressors of political violence as risk factors for substance use among adolescents.
Financial Support: The Israel trauma coalition and the Israel Center for the reatment of Psychotrauma

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RELATIONSHIP BETWEEN ESTRADIOL AND MOOD IN WOMEN SMOKERS.

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Aims: Smoking behavior and mood symptoms vary across the menstrual cycle in regularly menstruating women. The relation between smoking, mood, and ovarian hormones may be particularly relevant when women attempt to quit smoking. However, the association between ovarian hormones and mood has never been studied among nicotine dependent women. The purpose of this research was to examine the influence of estradiol on mood symptoms among regularly menstruating nicotine dependent women (N=55) over the course of a 6-week smoking cessation clinical trial. It was hypothesized that estradiol levels would be negatively associated with mood symptoms within participants.
Methods: Plasma estradiol levels and mood symptoms were assessed at two pretreatment sessions and at weekly study visits during a smoking cessation clinical trial for a total of 8 time points. Mood was assessed using the Beck Depression Inventory (BDI) and Premenstrual Assessment Form (PAF). Associations between estradiol levels and mood symptoms were calculated for each participant. Correlations were combined using meta-analytic techniques to yield an overall effect size and level of significance.
Results: There was a significant negative association between estradiol levels and PAF scores (r=-0.15, p=.02) over the course of the study. There was no association between estradiol levels and BDI scores.
Conclusions: Nicotine dependent women experience increased negative mood symptoms as estrogen levels decline, which is consistent with previous research in non-nicotine dependent women. In this study, the PAF was more sensitive to changes in ovarian hormones than the BDI. Improved awareness of predictable increases in mood symptoms could be used to enhance behavioral interventions for smoking cessation.
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N-ACETYLCYSTEINE CHANGES GLUTAMATE LEVELS IN COCAINE-DEPENDENT SUBJECTS: AN OPEN LABEL MAGNETIC RESONANCE SPECTROSCOPY STUDY.

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Aims: Treatment with N-acetylcysteine (NAC) restores glutamate homeostasis and prevents relapse in animal models. The aim of the current study is to investigate glutamate changes in the anterior cingulate cortex after an acute administration of NAC, measured by Proton Magnetic Resonance Spectroscopy in cocaine dependent human subjects compared to healthy controls.
Methods: In a within-subject, open label pilot study, 9 cocaine dependent subjects (CD) and 9 healthy controls (HC) underwent two scanning sessions: one following acute administration of NAC (2400 mg) and one receiving no compound (baseline). Localized proton magnetic resonance spectroscopy was performed with an MRS voxel placed in the left anterior cingulate cortex. Spectra were acquired using first order iterative shimming, a PRESS (TE/TR=38/2000 ms) and 64 signal acquisitions. Glutamate (Glu) concentrations were obtained using LCModel.
Results: Baseline Glu concentrations were significantly higher in the CD group compared to the HC group [T(16)=4.61, p<0.01]. After administration of NAC, both groups did not differ with respect to Glu levels [T(16)=0.05, p=0.96]. NAC significantly reduced Glu levels in the CD group [T(8)=4.15, p<0.01], whereas NAC had no effect on in the HC group [T(8)=-1.80, p=0.11]. Within the CD group, we found a positive correlation between duration of abstinence and Glu concentrations at baseline (r=0.62).
Conclusions: Elevated glutamate levels in CD compared to HC in the left dorsal part of the ACC normalized after administration of NAC. These findings could have important implications for treatment, because disturbed glutamate concentrations have been related to relapse in animal studies and treatment with NAC to prevention of relapse. In addition, the current study proves that MRS is a robust technique to detect changes in glutamate levels by glutamate mediating compounds such as NAC in the human brain.
Financial Support: ZonMw (Dutch Grant)

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MODAFINIL AND D-AMPHETAMINE FOR THE TREATMENT OF COCAINE DEPENDENCE.

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Aims: The literature for treatment of cocaine dependence supports research on the use of stimulants based on an "agonist substitution" model, similar to the use of methadone to treat opiate dependence. Two stimulant medications, modafinil and d-amphetamine, when tested individually, have shown safety and efficacy for cocaine addiction. This study hypothesized that the low dose combination of modafinil and d-amphetamine should have therapeutic potential by producing greater dopamine-enhancing effects via different mechanisms of action and with less exposure to the risks of each individual drug.
Methods: This double-blind, placebo-controlled randomized clinical trial compared 400 mg of modafinil to 60 mg of sustained release d-amphetamine to the combination of 200 mg modafinil and 30 mg of d-amphetamine in a sample of 72 subjects with cocaine dependence. Following assignment to one of the four treatment groups, subjects attended thrice weekly clinic visits, weekly individual therapy, and received study medication for 16 weeks. Cocaine use during treatment (urine benzoylecgonine) was the primary outcome measure in this preliminary report.
Results: A significant time by treatment interaction effect was driven by an increasing temporal trend in the probability of cocaine use for the combination (modafinil and d-amphetamine) and modafinil groups relative to placebo over time. d-Amphetamine did not demonstrate a difference relative to placebo. Using Bayesian modeling the combination group demonstrated an increase in the probability of attrition, resulting in low levels (< 20%) of treatment completion.
Conclusions: These findings fail to provide evidence of improvement with the medication combination of modafinil and d-amphetamine. Additional data on the safety of, and compliance with, this combination pharmacotherapy will be discussed in the context of future development of agonist-like medications.
Financial Support: National Institute on Drug Abuse Grant P50 DA09262

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CONTRIBUTION OF CORTICOSTERONE AND NEUROSTEROIDS TO THE EFFICACY OF METYRAPONE IN REDUCING COCAINE-RELATED BEHAVIORS.

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Aims: Several compounds which potentiate GABA-induced inhibitory currents can also decrease stress, anxiety and addiction-related behaviors. Also, previous findings from our lab suggest a role for HPA axis activation in potentiating cocaine-related behaviors. Metyrapone, a corticosterone synthesis inhibitor, decreases cocaine self-administration and cue-induced reinstatement but the mechanism is unclear. We hypothesize that metyrapone can decrease cocaine-related behaviors via increased biosynthesis of GABA-active neurosteroids such as allopregnanolone.
Methods: Male Wistar rats, trained to self-administer cocaine and food under concurrent alternating FR4 schedule, were used to elucidate this mechanism. Following the construction of a metyrapone dose-response curve in intact rats, bilateral adrenalectomies were performed and metyrapone was re-tested in each animal. Finasteride was administered in two injections of 100 mg/kg separated by 24 hours, starting 48 hours prior to the test session.
Results: Metyrapone was able to selectively decrease cocaine self-administration without affecting circulating corticosterone levels. Adrenalectomy also increases the efficacy of metyrapone, even in the absence of plasma corticosterone, suggesting a major mechanism beyond corticosterone synthesis inhibition. Pretreatment with finasteride (5alpha-reductase inhibitor) to decrease GABA-active neurosteroids partially attenuated metyrapone's efficacy, confirmed by one-way ANOVA. As well, administration of exogenous allopregnanolone decreased the cue-induced reinstatement of cocaine-seeking behavior.
Conclusions: These results suggest that the efficacy of metyrapone in reducing cocaine-related behaviors is unrelated to plasma corticosterone. Rather, GABA-active neurosteroids might mediate these effects. Further exploration of the indirect, GABAergic effects of metyrapone is needed.
Financial Support: DA 06013

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RISK EVALUATION AND MITIGATION STRATEGIES: NEW CHALLENGES AND OPPORTUNITIES FOR DRUG ABUSE INVESTIGATORS.

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Aims: Risk Evaluation and Mitigation Strategies (REMS) are now required for many pharmaceutical products having safety risks, including the risk of misuse, abuse, overdose, addiction and diversion. We will describe the emerging opportunities and potential roles for researchers in the implementation of Risk Evaluation and Mitigation Strategies (REMS), as well as potential challenges.
Conclusions: REMS include three phases: the premarketing risk assessment, implementation of the REMS, and the evaluation of the REMS. In the premarketing phase, animal and human abuse liability studies are required to determine whether or not a CNS product has abuse potential. Analysis of abuse-related data from clinical efficacy and safety trials is also needed. During the implementation phase, programs may be required to educate patients and healthcare providers of the potential risks associated with abuse and overdose of the new drug and how to prevent such events. During the evaluation phase, epidemiological research is needed to determine whether or not the REMS is effective at minimizing the abuse, diversion, and overdose associated with the drug.
REMS also provides new research challenges. Of primary importance are strategies to minimize abuse and diversion of the pharmaceutical drug among abusers, without inhibiting access to the drug for patients with legitimate medical needs. Other challenges include the development and introduction of drugs with novel mechanisms of action and new formulations of existing drugs, and measuring the impact of these products on misuse, abuse, overdose, addiction, and diversion.
Financial Support: Pinney Associates provides risk management services for several pharmaceutical companies. However, all financial support was from Pinney Associates, and no support from pharmaceutical comanies was, or will be, used to support this paper.

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RECEPTOR SUB-TYPE SELECTIVITY AFFECTS SUBJECTIVE AND COGNITIVE EFFECTS OF GABA MODULATORS IN HUMANS: A COMPARISON OF LORAZEPAM AND A NOVEL GABA-Aα2/GABA-Aα3 SELECTIVE MODULATOR.

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Aims: Non-selective GABAA benzodiazepine-site agonists have anxiolytic effects but also sedative, cognitive and abuse/dependence liabilities. The novel putative anxiolytic, AZD7325, is functionally selective for GABAAα2 and GABAAα3 subtypes and is associated with less sedation, less cognitive impairment and fewer reinforcing effects in animals. It was hypothesized that AZD7325 would have less abuse potential and cognitive effects compared to lorazepam in humans.
Methods: Randomized, double-blind crossover study with single doses of AZD7325 (10, 40 and 80 mg) compared to placebo and lorazepam (1.5, 3 and 6 mg) in adult healthy recreational CNS depressant users. Subjective (visual analogue scales [VAS]; Subjective Drug Value [SDV]; Addiction Research Center Inventory [ARCI]) and cognitive assessments (Choice Reaction Time [CRT]; Divided Attention [DA]; Hopkins Verbal Learning Test-Revised [HVLT-R]) were administered over 24 hours. The primary endpoint (peak Drug Liking VAS) and secondary endpoints were analyzed using mixed-effect models.
Results: 35 subjects were randomized and 28 completed the study. Peak Drug Liking values for all doses of lorazepam and AZD7325 were significantly greater than placebo ($p \leq 0.041$). While AZD7325 10 mg was not significantly different from lorazepam 1.5 mg ($p=0.997$), all AZD7325 doses showed significantly lower peak Drug Liking versus lorazepam 3 and 6 mg ($p \leq 0.023$). Dose-effect relationships for AZD7325 were shallower than lorazepam. Secondary endpoints showed a similar pattern of results. Unlike lorazepam, AZD7325 did not significantly impair cognitive/motor performance.
Conclusions: Although AZD7325 showed some abuse potential compared to placebo, the results support the hypothesis that single doses of AZD7325 have less abuse and cognitive impairment potential than the full GABAA agonist, lorazepam, in recreational drug users.
Financial Support: The study was funded by AstraZeneca.

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MEDICAL CARE UTILIZATION IN A METHAMPHETAMINE-DEPENDENT TREATMENT FOLLOW-UP SAMPLE.

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Aims: Methamphetamine (MA) abuse remains a major health care problem in the United States, causing a wide array of medical and psychiatric problems. As a result, MA users utilize more hospital resources than non-MA users, especially those offered in emergency or urgent care settings (London et al, 2009). MA users are more likely to be admitted into the hospital than non-MA users (Richards et al, 1999; Hadjizacharia et al, 2007), thus requiring a larger percentage of available health care resources and funding.
Methods: Secondary data analysis includes 587 MA-dependent individuals who participated in the "Methamphetamine Treatment Project" (MTP), and completed the 3-year post-treatment follow-up assessment. Comparisons were made between participants distinguished by urine test results at the 3-year follow-up (MA-positive vs. MA-negative) to examine the association between hospital utilization and MA use. Data were collected with a study-specific Hospital Utilization & Access to Care survey, which addressed general health, recent medical care, and hospital visit information.
Results: Results indicate significant differences in sources of usual medical care by MA-negative (n=406) and MA-positive (n=181) groups. 50% of MA-negative participants and 36% of MA-positive participants report seeking care from a doctor's office or HMO ($p=0.001$). Similarly, only 15% of MA-negative participants but 25% of MA-positive participants reported most often seeking medical care from a Hospital ER ($p=0.004$). Current MA use also distinguishes other items including self-ratings of health status ($p=0.001$), and improvement in health ($p=0.0001$)
Conclusions: These findings highlight the costs related to MA use, and emphasize the need for effective MA prevention and treatment efforts.
Financial Support: CSAT 270-01-7089

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UPREGULATION OF ENDOCANNABINOIDS ATTENUATES THE PRO-EMETIC EFFECTS OF OPIATES.

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Aims: Opiates are associated with unwanted side effects such as nausea and emesis that decrease compliance and affect patient quality of life. Exogenous cannabinoids can mitigate these effects, but are problematic for numerous reasons. An alternate strategy may be to upregulate endogenous cannabinoids such as anandamide. We determined if LY2183240, an inhibitor of anandamide's metabolism and reuptake, is effective in attenuating the pro-emetic pica response and activation of relevant brainstem nuclei induced by the opiate oxycodone. We also assessed whether it affected the antinociceptive action of oxycodone or activated neural reward areas.
Methods: Adult male and female Sprague-Dawley rats were administered varying doses of LY 2183240 (ip) 30 min prior to oxycodone (15 mg/kg; oral). The pro-emetic pica response was measured by incidents of cage bedding intake. Underlying neural activation was assessed by c-fos positive neuron counts in the brainstem area postrema and nucleus of the solitary tract. We used the hotplate to assess the antinociceptive action of LY2183240 alone and in combination with oxycodone. We also assessed reward potential by measuring c-fos positive neurons in the nucleus accumbens.
Results: LY2183240 dose-dependently decreased oxycodone-induced pica in male rats. In females it had no effect on oxycodone-induced pica and at high doses it induced pica. LY2183240 decreased the number c-fos positive neurons in the brainstem pro-emetic neural circuitry oxycodone. LY2183240 had no antinociceptive action on its own and did not affect oxycodone-induced antinociception. LY2183240 did not activate reward neural circuitry, as there was no increase in the number of c-fos positive neurons in the nucleus accumbens.
Conclusions: Upregulating synaptic levels of endocannabinoids may be a useful strategy to combat the adverse side effects associated with prescription opiates, especially since it does not appear to affect the analgesic action of opiates or induce reward. More study is needed to determine the role that gender plays.
Financial Support: LSUHSC-S Intramural Research Award
USPHS DA018181 (NIDA, NIH)

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CHILDHOOD TRAUMA, SUBSTANCE USE, AND MENTAL DISORDERS PATTERNS AMONG HOMELESS IN BRITISH COLUMBIA.

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Aims: International and Canadian studies have indicated that homeless populations suffer from high rates of substance use disorders, physical health problems and psychiatric illnesses. However, few studies have included standardized assessments to elucidate the prevalence of Axis I diagnosis in this marginalized population. To fill this gap, we examined lifetime and current diagnoses of mental and substance use disorders, as well as childhood traumatisation.
Methods: A total of 500 homeless British Columbians were interviewed. Participants living on the street, or in shelters were recruited from the cities of Vancouver, Victoria and Prince George. Care was taken to assemble a representative sample. Standardized assessments included the Mini International Neuropsychiatric Interview (MINI Plus), the Maudsley Addiction Profile and the Childhood Trauma Questionnaire.
Results: Mean age was 37.9 (SD: 11.0); 39.2% were female; and 39.8% of aboriginal descent. The lifetime prevalence of alcohol (68.9%) and illegal substance dependence (76.5%) were high, as were lifetime mental illnesses: major depression episodes (45.4%), manic episodes (44.4%) and psychosis (27.2%). Mental disorders were significantly associated with elevated use of specific substances. A lifetime diagnosis of depressive episodes was significantly associated with increased alcohol ($p=0.03$) and illicit benzodiazepine use ($p=0.03$). Manic episodes were associated with increased use of cannabis ($p=0.0001$) and illicit opiods ($p=0.007$) and psychotic disorders with elevated use of illicit benzodiazepines ($p=0.04$), amphetamines ($p=0.04$), and crystal methamphetamine ($p=0.005$). Levels of childhood traumatisation were specifically high in individuals reporting manic episodes.
Conclusions: Extremely high prevalence of substance use (disorders) and sever mental health disorders were recorded in homeless population in British Columbia. Childhood trauma was associated with specific substance dependence and mental disorders. Potential pathways of early traumatisation with substance use and mental disorders will be discussed.
Financial Support: Province of British Columbia

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COMPARISON OF BUPRENORPHINE AND METHADONE TREATMENT AMONG MEDICAID ENROLLEES.

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Aims: The availability of buprenorphine treatment for opioid dependence has expanded medication assisted treatment options, yet little is known about the use of buprenorphine (Bup) in a Medicaid managed care organization (MCO). The purpose of this study was to examine the characteristics and treatment retention of Medicaid enrollees prescribed Bup versus being treated with methadone (Meth) maintenance.
Methods: Four years of medical claims data (2006-2009) were used to identify enrollees initiating Bup or Meth opioid dependence treatment. This intention-to-treat analysis grouped members by initial type of treatment. Chi-square and t-tests were used to compare demographic and health status characteristics. Cox proportional hazards models were used to examine treatment retention during the 12-months after treatment initiation.
Results: 1,021 unique enrollees treated for opioid dependence were identified; 38% initiated Bup treatment. Compared to Meth, those on Bup were significantly ($p<0.05$) more likely to be white (50 vs 43%), from rural areas (21 vs 9%), and diagnosed with the following co-occurring conditions: psychiatric disorder (49 vs 32%), renal disease (18 vs. 10%), respiratory illness (10 vs 6%), and to have cocaine abuse/dependence (24 vs 6%), and alcohol abuse/dependence (18 vs 2%). For Bup, rural living (vs. urban, HR=1.6, $p<0.03$), younger age (vs. age>50, HR=1.5, $p<0.02$), being HIV+ (HR=1.5, $p<0.04$), having a psychiatric diagnosis (HR=1.4, $p<0.02$) and respiratory diagnosis (HR=1.7, $p<0.03$) were each associated with a greater risk of dropout. Analyses comparing Bup to Meth indicate that those on Bup had a significantly greater risk of dropout (HR=1.5, $p<0.05$) controlling for group differences.
Conclusions: In this sample of Medicaid MCO enrollees, those on Bup had a different demographic profile and higher rates of comorbidities than those on Meth. Controlling for these differences, retention in treatment was significantly lower for the Bup group.
Financial Support: None

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ENTRY INTO METHADONE TREATMENT VIA INTERIM MAINTENANCE: 12-MONTH OUTCOMES.

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Aims: To compare the effectiveness of three levels of counseling over a one-year period for new admissions to two Methadone Treatment Programs (MTPs).
Methods: New adult MTP admissions were randomly assigned to one of three treatment Conditions: Interim Methadone (IM – emergency counseling only for the first 120 days) v. Standard Methadone (SM – counseling as usual) v. Restored Methadone (RM – counseling with a reduced case load, available at only one of the MTPs). The Addiction Severity Index (ASI) and urine drug testing were administered at treatment entry, and 2-, 4-, and 12-month follow-up. All patients received regular drug counseling after 120 days. Analyses will be conducted to examine changes over 12 months using Poisson regression and Generalized Estimating Equations.
Results: 230 participants were enrolled: mean age, 43.2 years old; male, 70%; African American, 77.4%; and White, 21.3%. There were no significant differences among Conditions at baseline in terms of demographics or the number of self-reported days of heroin (29.1 days) or cocaine (5.8 days) use. To date we have located 97% and interviewed 90% of the 210 participants who are one year post-entry. At the 4-month follow-up there were no significant differences favoring groups who received regular or restored methadone maintenance. 12-month findings will be reported on the entire sample for self-reported drug use, drug tests, retention in treatment and criminal behavior.
Conclusions: If 12 month results confirm the 4-month findings, findings would suggest that drug counseling as it is delivered in Baltimore is either inadequate in quantity or quality, or that the effect of methadone in this population is so robust that any incremental effect of counseling cannot be demonstrated. Results may have implications for the regulatory and clinical structure of methadone treatment in the US.
Financial Support: NIDA DA R01 013636

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INDIVIDUAL CHARACTERISTICS AND RESPONSE TO CONTINGENCY MANAGEMENT TREATMENT FOR COCAINE ADDICTION.

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Aims: The development and dissemination of effective treatments for cocaine dependence is an important public health priority in Spain. Behavioral interventions that include contingency management (CM) have obtained positive results for cocaine addiction, but few studies have examined associations between individual baseline characteristics and response to CM treatments. This study evaluated the effect of individual baseline characteristics on six months-outcome in an outpatient CM program for cocaine addicts.
Methods: Participants were 50 subjects who received a treatment based on CM. The patients received incentives contingent on cocaine abstinence. A logistic regression analysis was conducted to examine the usefulness of baseline participants' characteristics (independent variables) in predicting likelihood of cocaine abstinence at six months of treatment (dependent variable).
Results: The rate of patients who were abstinent after six months of treatment was 58%. Patients with higher scores on the Alcohol area of the EuropASI and that use cocaine during the first month of treatment were less likely to achieve abstinence. The rest of baseline variables examined (sociodemographic variables, drug use variables, psychopathological profile and psychological functioning) were not statistical significant predictors of abstinence.
Conclusions: This finding is important to direct CM approaches to patients most likely to benefit and for the generalizability of CM across patients with different characteristics.
Financial Support: Spanish National Plan on Drugs (Ref. MSC-06-01) and the University of Oviedo, Spain.

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PAIN IN METHADONE MAINTENANCE PATIENTS.

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Aims: Cross-sectional study to examine pain in methadone maintenance patients.
Methods: 143 subjects were recruited from NYC methadone programs, asked about cravings for opioids and the following tools were administered: Brief Pain Inventory (BPI) and Memorial Pain Assessment Card (MPAC) Pain Scale, Addiction Severity Index Lite, Brief Symptom Inventory.
Results: 58% men, mean age=48,SD 8.7, 58% Black, 28% Latino, 8% White, 4% Native American, 2% other. Mean methadone dose=88mg,SD 38. MPAC pain scale positively correlated with BPI composite, r=.58,p<.01 and BPI pain interference, r=.52,p<.01 scores. Number of days/month of medical problems predicted pain on BPI, b=.48,t(141)=6.53,p<.01. 34.7% reported pain 50/100 or higher, 13.2% reported 75/100 or higher. Men and women report pain equally across all age groups. Report of pain significantly differed by ethnicity, Native Americans reported the highest levels and Whites the lowest, F(4, 138)=2.77,p=.03. Subjects with pain were on higher doses of methadone, BPI score predicted methadone dose, b=.23,t(141),p=.05. The degree patients felt free from drug cravings positively correlated with negative toxicology results in the past 12 months r=.224,p=.007. A negative correlation between negative toxicology and depression, r=-.214,p=.01, somatization, r=.176,p=.036 and phobic anxiety, r=-.182,p=.03 was detected. Negative toxicology did not correlate with pain, r=-.096,p=.255. BPI composite scores positively correlated with refusal of a toxicology screen, r=.197,p=.018. Pain severity positively correlated with anxiety, r=.2,p=.017 and somatization, r=.32,p<.01.
Conclusions: Pain from multiple medical problems is prevalent in methadone maintained patients and interferes with activities. Refusals for toxicology screening may indicate greater illicit drug use in patients with pain. Patients with pain were on higher doses of methadone which may be useful managing pain. Federal regulations do not permit programs to dispense methadone for pain management and may need to be reconsidered.
Financial Support: Baron Edmond De Rothschild Chemical Dependency Institute

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UPDATE ON FORMULATIONS TO DETER TAMPERING.

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Aims: To summarize progress since the 2005 CPDD Conference *Impact of Drug Formulation on Abuse Liability, Safety and Regulatory Decisions* (DAD 2006; 83 suppl 1).
Results: Although several formulations that deter tampering have been approved since 2005, recurring issues in the development of these products remain. These include: misunderstanding about what factors decrease the likelihood of tampering/abuse and how individuals may tamper with a drug; lack of clarity about what data are appropriate to support implicit or explicit label claims; the relative weight assigned to in vitro and clinical studies; failure to adapt the experimental approach to the specific formulation (eg, antagonists vs physical deterrents); assumption that kinetic differences are sufficient to infer clinical differences; reluctance to include all the proper conditions in clinical or in vitro studies that support the labeling goals; failure to address the impact on patients/prescribers.
Companies understand that an explicit abuse deterrent claim can be achieved only with product-specific postmarketing data showing an impact on relevant health outcomes. However, existing postmarket databases and study designs have many limitations, most notably a lack of product specificity and the fact that most abuse related adverse outcomes are infrequent for small market-share products and study durations become unacceptably long.
Conclusions: Most tamper modifying technologies move behaviors toward decreased postmarket risk. Since proving product-specific abuse deterrence in the market will be elusive, labels could describe physical properties (eg, gel-forming) combined with clinical abuse liability data to accurately test the formulation's intent. Such labeling informs physicians and patients without overly inferring abuse resistance or presenting instructions for abuse. Confirmation of public health benefit may require large nationally sponsored studies. However, development of tamper deterrent products needs continuing regulatory support so that tamper-deterrent products become the expected standard for certain drug classes.
Financial Support: Kendle Toronto.

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THE EFFECT OF THE CB1 NEUTRAL ANTAGONIST PIMSR1 ON APPETITIVE DISORDERS.

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Aims: To assess whether PIMSR1, a neutral antagonist of the cannabinoid CB1 receptor, attenuates cocaine-enhanced brain reward or food self-administration.
Methods: Computational modeling and synthesis to provide test compounds. Electrical brain stimulation reward (BSR) threshold assay to determine attenuation of cocaine-enhanced brain reward. Food intake studies in mice to determine effect on eating.
Results: The ligand PIMSR1, which was designed to lack a H-bonding interaction that would stabilize the inactive state of the CB1 cannabinoid receptor, was shown to have high affinity for hCB1 (Ki = 17 nM) and to be a neutral antagonist by calcium channel assay. BSR assay demonstrated a significant attenuation of cocaine enhanced brain reward over a range of concentrations. Also demonstrated was the absence of a dysphoric response from PIMSR1 itself, in contrast to that exhibited by rimonabant. Food intake was examined under the influence of PIMSR1.
Conclusions: Neutral antagonism of the CB1 receptor affords receptor blockade that results in attenuation of cocaine-enhanced brain reward in rats while at the same time exhibiting no dysphoria. 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.
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PRENATAL TOBACCO USE AND MENTAL HEALTH CONDITIONS IN WOMEN AT RISK FOR OTHER SUBSTANCE USE.

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Aims: Smoking during pregnancy is the most modifiable risk factor for poor birth outcomes & is linked to poor outcomes for mother and child (CDC 2001). Smoking rates during pregnancy have been declining (Colman 2003) yet remain high among low SES women (Tong 2009). Mental health (MH) conditions & high stress levels increase odds of continued smoking (Holtrop 2009). This study examined relationships between prenatal & lifetime cigarette smoking & an array of MH symptoms in a sample of pregnant women screened at risk for prenatal substance use.
Methods: Recruitment occurred in an urban hospital-based prenatal clinic in Richmond, VA. Participants: N=155 English speaking pregnant women, > 18 years screening at risk for alcohol/drug use. Those consenting completed a baseline assessment as part of an ongoing clinical trial on HIV/STD risk reduction. This study focused on demographic, alcohol/drug & psychological domains of the ASI, with additional items on cigarette smoking. Women were categorized into 3 groups: nonsmokers (NS, n=39), past daily smokers (PDS, n=34) & continued smokers (CS, n=56). Chi-square & ANOVA analyses were used to compare demographic, substance use and recent (past 30 days) as well as lifetime MH measures.
Results: Women were 85% AA, mean age 26, 72% welfare recipients. There were no significant differences among the 3 groups for recent or lifetime MH measures. When comparing PDS to CS, the CS reported significantly higher levels of current anxiety (55.4% vs 32.4%, p=.034) & recent cognitive problems (30.4% vs 8.8%, p=.017) than the PDS. No significant differences were found for lifetime MH symptoms between the 2 groups. Significant differences were also noted between CS & PDS with regard to illicit drug use ($p<.05$).
Conclusions: Findings suggest greater MH needs among low SES, pregnant smokers are associated with the short term/during pregnancy & that CS may turn to substance use as a coping strategy. Pregnancy presents a window of opportunity for substance use intervention; specialized strategies for this population are needed.
Financial Support: NIH 1P60MD002256-01 U10 DA13034

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EFFECTS OF CROSS-DRUG PREEXPOSURE ON COCAINE- AND VANOXERINE-INDUCED CONDITIONED TASTE AVERSIONS.

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Aims: Although cocaine readily induces taste aversions, little is known about the mechanisms underlying this effect. Since cocaine is a nonselective monoamine transport inhibitor, it has been suggested that its effects at one of the monoamines may be mediating this suppression. The present series of studies used the cross-drug preexposure design to determine if vanoxerine (GBR 12909), a selective dopamine (DA) transporter inhibitor, and cocaine induce aversions by a common mechanism, specifically increases in DA activity.
Methods: Male Sprague-Dawley rats were exposed to GBR 12909 (32 mg/kg) prior to aversion conditioning with cocaine (18 mg/kg), GBR 12909 (32 mg/kg) or vehicle. GBR 12909 and cocaine were administered subcutaneously.
Results: A 2 x 3 x 4 mixed-model ANOVA revealed significant effects of Trial, Preexposure drug and Conditioning drug, as well as significant Trial x Preexposure drug and Trial x Conditioning drug interactions. That is, regardless of conditioning drug, there were differences between subjects preexposed to GBR 12909 and those preexposed to vehicle across trials. Additionally, regardless of preexposure condition, there were differences between subjects conditioned with cocaine, GBR 12909 and vehicle across trials. A One-way ANOVA on the Final Aversion Test revealed significant group differences. Fisher LSD post hoc analysis revealed that preexposure to GBR 12909 attenuated aversions induced by itself, but had no effect on cocaine-induced aversions.
Conclusions: Since cocaine-induced CTAs were not attenuated by GBR 12909 preexposure (whose major action is inhibition of DA reuptake), it is unlikely that DA plays a significant role in aversions induced by cocaine.
Financial Support: This research was supported by a Grant from the Mellon Foundation to ALR.

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MODELS OF INTERORGANIZATIONAL CHANGE FOR IMPLEMENTING EBPS IN CORRECTION-PROVIDER NETWORKS.

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Aims: Cooperative interplay between correctional agencies and drug treatment agencies is critical in the effective management and treatment of offenders with substance use disorders. The Criminal Justice Drug Abuse Treatment Studies research cooperative is evaluating the implementation of evidence supported treatment in three treatment areas: medicated assisted treatment (MAT), assessment and case planning, and HIV services. Primary mechanisms of change in all three studies are that of an inter-agency change team and the introduction of a facilitator. We will overview the research protocols and highlight the functional distinctions in the composition, characteristics, and critical ingredients of the organizational change processes (local change teams and facilitators).
Conclusions: These change processes can be differentiated by the location of the facilitator or change agent (internal vs. external to participating organizations), the identification of implementation targets for the local change team (externally imposed versus change team identified) and the relative "dosing" or type and amount of support provided by the facilitator. While CJDATS does not allow for a comparative analysis of each of these implementation factors, each has precedent in the organizational change literature and each carries with it implied assumptions related to establishment and sustainment of inter-organizational change processes that promote the utilization of evidence supported approaches in the management and treatment of offenders with substance use disorders.
Financial Support: This study was funded by a cooperative agreement from the U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse (NIH/NIDA). No financial conflicts exist for any of the authors.

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FUNCTIONAL MRI-BASED SUPPORT VECTOR MACHINE CLASSIFICATION OF TOBACCO SMOKERS' NICOTINE CRAVING: POSSIBLE USE IN REAL-TIME NEUROFEEDBACK.

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Aims: Pattern classification offers a novel way to evaluate neuroimaging data. Support vector machine (SVM) classification is a learning algorithm that has been used to classify fMRI data. Studies show that nicotine dependence level is associated with greater BOLD fMRI activation and cigarette craving in response to smoking cues. This study explores SVM classification as a potentially sensitive tool to investigate neural processes involved in craving.
Methods: T2*-weighted data were acquired on a 3T GE scanner using a custom spiral-in sequence (TR/TE/FA/FOV=2s/30ms/90/22cm, 64x64 matrix, 40 axial slices of 3mm thickness). At screening, we measured expired CO, Fagerstrom dependence level, and daily cigarette use to ensure at least moderate smoking. Subjects were scanned after overnight abstinence. The paradigm involved two runs of pictures depicting smoking- and non-smoking stimuli that, accordingly, were more or less likely to prompt craving (20s blocks of 5 pictures for 4s each, 16 repeats, with 4s fixation between blocks, 384s total time). SVM training and testing were done using 3dsvm in AFNI. Linear kernel was used for classification. A brain mask was used to exclude non-brain voxels. The model trained on run1 was used to test run2, and vice versa.
Results: Ten subjects completed: 5M/5F, mean age=24.7 yrs, mean Fagerstrom=4.1, cigarette use range: 8-20/day, mean CO (ppm)=17.6 (screening) and 5.8 (pre-scan). Mean prediction accuracy values were 66.6% and 66.8% for training runs 1 and 2 respectively (range across subjects and runs: 51.3–85.6%). Based on the mean prediction vector, effect size (Cohen's d) was 2.31.
Conclusions: We successfully demonstrate an SVM algorithm to classify smokers' cue-reactivity to visual smoking and non-smoking cues. By exploiting the fast nature of SVM (i.e. every TR), these findings encourage possible implementation of real-time neurofeedback to help subjects control their nicotine craving.
Financial Support: Supported by NIH R01 DA026077 and Joe Young, Sr. Funds (State of Michigan)

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THE FEASIBILITY OF PROVIDING EDUCATIONAL COUNSELING FOR HEROIN ABUSERS PARTICIPATING IN NEEDLE-SYRINGE EXCHANGE PROGRAMS IN PENANG, MALAYSIA.

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Aims: Providing education on viral infections and treatment opportunities enhances harm reduction effectiveness of NSPs. We are evaluating the feasibility of providing an extended and structured EC program to non-treatment seeking, active drug injectors utilizing informal NSPs in Penang State, Malaysia by measuring the EC treatment adherence, reported reductions in behavioral risks, and rates of enrolment in formal and structured treatment programs.
Methods: A total of 124 active heroin injectors participating in NSP were evaluated and 96 of them met the entry criteria and volunteered to enter a 10 session EC program, followed by 3 monthly follow-up visits. EC is offered in group settings.
Results: 84/96, (88%) participants are male with the mean (SD) age of 42.6 (10.4) years. The means (SD) of their durations of heroin abuse and injection drug use were 20.7 (10.3) and 11.3 (9.3) years respectively. Overall, 62.5% of the sample reported or tested positive for one or more other drugs: 34% methamphetamine, 25% benzodiazepines, and 23% cannabis. Despite efforts of the research team to maintain phone contact with all study participants 33/96 (34%) of participants never attended a single EC session, while 29/96 (30%) attended 5 or more sessions (active participation). 15/96 (16%) of the participants joined a Medication Assisted Treatment (MAT) during the study period: 9/29(31%) of those who actively participated in EC, compared to 6/67 (9%) of non-active participants ($p<0.05$).
Conclusions: Despite successful engagement of non-treatment seeking drug injectors, only 1/3 of them actively participated in the offered EC program. While our data shows a positive relationship between active participation in an EC and joining MAT, this ongoing feasibility study conducted in naturalistic environment does not afford careful interpretation regarding detailed reasons for entering or not entering MAT by non-treatment seeking drug injectors in Malaysia.
Financial Support: Short-term grant, Universiti Sains Malaysia

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FACTORS ASSOCIATED WITH SUBSTANCE ABUSE TREATMENT ENTRY AMONG RURAL, APPALACHIAN DRUG USERS IN KENTUCKY.

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Aims: Research suggests multiple factors (i.e., socio-demographic, health, substance use, and previous treatment) may influence treatment entry. This study examines factors associated with substance abuse treatment entry among rural Appalachian drug users.
Methods: Data are from a community sample of drug users in rural Appalachia (N = 403). Baseline and six month follow-up data were recorded via an interviewer-administered questionnaire.
Results: Over half of participants were male (57%), the median age was 30.5 years. Consistent with the population in rural, Appalachian Kentucky, the majority were white (93.5%). Of the 403 participants, 45 (11%) reported receiving substance abuse treatment between the baseline and follow-up interview. Being enrolled in a 12-step (39%), outpatient (33%) or residential (33%) program were the most common modalities. Multivariable logistic regression was used to examine the predictors of treatment entry. Socio-demographic characteristics (i.e., age, race, education, insurance), health status (i.e., physical health, depression, anxiety), substance use in the past 30 days and related problems (i.e., degree of trouble, criminal justice involvement), and previous treatment episodes were examined. Multivariable analysis showed that individual's perceptions of treatment importance (AOR: 3.68, 95% CI: 1.91, 7.07) and education (AOR: 1.02, 95% CI: 1.01, 1.04) predicted treatment entry, while oxycodone use in the 30 days prior to the baseline interview (AOR: .038, CI: .20, .73) was negatively associated with treatment entry.
Conclusions: Findings suggest that socio-demographics, perceptions of treatment importance, as well as recent substance use can all be important factors in the decision to pursue substance abuse treatment. Understanding predictors of substance abuse treatment entry for individuals living in rural, Appalachia presents important opportunities to incorporate this knowledge into prevention and treatment efforts.
Financial Support: This research is supported by: NIH/NIDA R01DA024598 (PI: Jennifer Havens).

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SYNTHESIS OF M-100907 A 5-HT2AR ANTAGONIST AND WAY-163909 A 5-HT2CR AGONIST ANALOGS.

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Aims: Previous studies indicate that the 5-HT2AR and 5-HT2CR play a role in cocaine induced behavior modification through either stimulation or inhibition respectively, and these receptors may dimerize in-vivo. Bivalent ligands have been shown to possess increased affinity and potency when compared to administration of the monomers. The aim of this project is to synthesis homodimeric 5-HT2A R antagonists, homodimeric 5-HT2CR agonists, and heterodimeric 5-HT2A R antagonist/5-HT2CR agonist that will exhibit improved ability to control cocaine induced behavior modifications compared to the concurrent administration of a 5-HT2A R antagonist and a 5-HT2CR agonist.
Methods: Derivatives of the 5-HT2A R antagonist M-100907 and the 5-HT2CR agonist WAY-163909 will be synthesized to determine optimal binding site and the appropriate linker location. Dimers containing linkers of various lengths are then synthesized to determine optimal linker length. The dimers are then assayed to determine if they exhibit increased affinity and potency at the 5-HT2CR and the 5-HT2AR.
Results: The appropriate linker attachment site has been determined for the 5-HT2AR antagonist M-100907, and the first set of 5-HT2AR antagonist homodimers have been synthesized and tested. Derivatives of the 5-HT2CR agonist WAY-163909 have been synthesized and are in currently being assayed to determine the appropriate linker site.
Conclusions: Homodimeric bivalent 5-HT2AR ligands and WAY-163909 derivatives containing a pseudo-tether have been synthesized. These homodimeric ligands may lead to novel bivalent ligands with improved affinity and potency at their targeted receptors.
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Agency: NIDA. Type:P20(DA 024157)09/30/2007-07/31/2011
Neural and Pharmacological Mechanisms of Action of Drugs of Abuse Johnson (PI) T32 DA 07287 07/01/2007-06/30/2012

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MORPHINE VACCINATION AND ITS INHIBITION OF MORPHINE-INDUCED CPP AND ANALGESIA IN RATS.

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Aims: Vaccination has great potential for becoming a useful clinical tool for the treatment of substance abuse. However, vaccines for heroin are in the early stages of development. This study investigated the effect of morphine vaccination on animal behaviors.
Methods: Sprague Dawley rats were immunized using 100 μg of morphine-succinyl-KLH conjugate mixed with 1500 μg alum and boosted after 3 weeks with the same dose. Anti-morphine antibody was evaluated at 2, 4, 6, 8 and 12 weeks after immunization by Elisa. The conditioned place preference (CPP) procedure was used to study the vaccine effects on reward responses to morphine (0, 1 or 2 mg/kg; S.C.). Morphine was paired with one chamber and saline with the other chamber for four training trials each using an unbiased procedure. Morphine (2mg/kg, S.C.) induced analgesia was also assessed using tail flick and hot plate assays.
Results: Anti-morphine antibodies were present in sera by 4 weeks, and maintaining at a high level by 8 weeks after immunization. Control rats immunized with KLH alone had no detectable morphine antibody at any time point. Morphine produced a significant dose-related place preference in KLH rats, which was reduced at the highest dose in immunized rats. This suggests that immunization of morphine vaccine partially blocked the acquisition of morphine CPP. Tail flick assays revealed that morphine induced analgesia was significantly reduced in immunized rats at weeks 7 and 9 ($P<0.01$), but the reduction was not statistically significant at 11 weeks. A similar inhibition of analgesic effect from morphine was demonstrable using a hot plate test, except that analgesia was significantly inhibited in immunized rats at each time point tested (7, 9, and 11 weeks, $p<0.05$).
Conclusions: In summary, this study has shown that the vaccination elicits specific antibody to morphine, which blocked morphine induced analgesia, and inhibited drug reinforcement (CPP).
Financial Support: R01 DA026859

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THE REINFORCING THERAPIST PERFORMANCE (RTP) EXPERIMENT: PRELIMINARY COST-EFFECTIVENESS FINDINGS.

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Aims: The Institute of Medicine has recommended rewarding provider performance to improve the quality of treatment, yet few experimental evaluations of such of such pay-for-performance (P4P) approaches exist. This study aims to test the hypotheses that the therapist incentives in the Reinforcing Therapist Performance (RTP) experiment are effective and cost-effective through their increase in outputs.
Methods: The Center for Substance Abuse Treatment (CSAT) funded over 30 substance abuse treatment agencies under contract HHSS270200700004C to implement the Adolescent Community Reinforcement Approach (A-CRA). The RTP study, supported by NIAAA R01AA017625, randomly assigned 29 participating CSAT agencies and their 105 participating therapists to either an experimental P4P condition or to implementation-as-usual (IAU). Therapists in the P4P condition received monetary bonuses for delivering a targeted threshold level of treatment (i.e., $200 per client achieving Target A-CRA) associated with significantly improved treatment outcomes and for demonstrating monthly competence in delivering A-CRA procedures (i.e., $50 per month of Monthly Competence, MC). Cost-effectiveness (Target A-CRA and MC per million dollars) was compared between conditions using multivariate regression, controlling for the site's average hourly wage of therapists.
Results: Bonuses cost $100 per client. Costs per client overall were similar in both conditions ($5998 in P4P $5792 in IAU). P4P increased both Target A-CRA and MC. Target A-CRA clients per million dollars in P4P was 3.4 times that in IAU (22.1 vs. 6.5, p=0.19, effect size d=0.57). MC per million dollars in P4P were 1.6 times that in IAU (41 vs. 25, p=0.08, d=0.47).
Conclusions: The limited number of facilities and substantial variability in costs per client limited statistical significance. Nevertheless, with moderate effect sizes on cost-effectiveness for both outcomes, P4P may be a promising and cost-effective method to improve the quality of substance abuse treatment for adolescents.
Financial Support: NIAAA (AA017625) and CSAT (HHSS270200700004C)

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THE EFFECTS OF AMPHETAMINE ON WORKING MEMORY IN RATS EXPOSED TO THE DRUG IN ADOLESCENCE COMPARED TO ADULTHOOD.

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Aims: Amphetamine (AMPH) use typically begins in adolescence and a strong association exists between adolescent-onset drug use, cognitive dysfunction, and a high lifetime prevalence rate of drug dependence. Also during this time, brain areas such as the prefrontal cortex (PFC) are undergoing significant, yet normal, changes in cellular structure and connectivity. As such, adolescents, compared to adults, may be especially sensitive to drug-induced plasticity. Here, we assessed the effects of AMPH exposure during adolescence or young adulthood on working memory in adulthood.
Methods: Male Sprague-Dawley rats were given 10 injections of saline or AMPH (1.0 or 3.0 mg/kg, i.p.), once every other day. This occurred when rats were adolescents (postnatal day (P) 27-45 or P37-55) or young adults (P85-103 or P90-108). After all rats reached adulthood (>P110), they were trained and tested in an operant-based, delayed matching to position (DMTP) task.
Results: Our preliminary results suggest that after the first injection of AMPH, there were no robust, age-dependent differences in locomotor activation at either dose. After the 10th injection, however, adults exhibited significantly more stereotypy (e.g., repetitive sniffing and head bobbing) compared to adolescents. In the DMTP task, rats that were exposed during adolescence exhibited more errors at long delays (12-24 sec) compared to saline-treated controls and those treated during adulthood. Notably, these behavioral tests occurred more than 1.5 and 3.5 months after the last AMPH injection in adult- and adolescent-exposed rats, respectively.
Conclusions: Whereas adolescent rats are less sensitive to the stereotypy-inducing effects of repeated AMPH exposure, they are more sensitive to its adverse effects on working memory. Because similar deficits in DMTP have been observed following disruptions of medial PFC activity, a potential mechanism for these effects on cognition is a heightened sensitivity of the developing adolescent PFC to AMPH-induced plasticity.
Financial Support: Arnold O. Beckman Award, UIUC

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A LATENT TRANSITION ANALYSIS OF CHILDHOOD MALTREATMENT AND PATTERNS OF ADOLESCENT SUBSTANCE USE.

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Aims: Childhood maltreatment has been linked to adolescent substance use in cross-sectional studies but the studies were unable to test the associations between childhood maltreatment and changes in substance use patterns during adolescence. We examined the linkages between exposure to childhood maltreatment and developmental trends of adolescent alcohol, cannabis, cocaine, opioid, and hallucinogen use.
Methods: We used the Patterns of Youth Mental Health Care in Public Service Systems Study dataset, a 3-year longitudinal study that includes 1,642 youth (mean age: 15.9 @ Year1), who were selected from five publicly-funded service systems. We performed mover-stayer latent transition analysis (LTA) to classify at-risk youth as movers and stayers based on their experience of illicit substance use over two years, examine transitions in substance use patterns across time, and explore how childhood maltreatment and gender relate to such change in substance use patterns over time.
Results: We identified a 3-class model of substance use (Bayesian information criterion(BIC)=1313.24; Lo-Mendell-Rubin adjusted likelihood ratio test:four classes p=.29; bootstrap likelihood ratio test:four classes p=.67). The 3 classes included: moderate alcohol/cannabis and no hard drug users (31%), high alcohol/cannabis and low hard drug users (11%), and heavy polysubstance users (58%). We found that the majority of adolescents (92%) do change patterns of substance use during the developmental period spanning 13-20 years of age. Mover-stayer LTA indicated that progression toward heavy polysubstance use increased with experience of childhood maltreatment. Findings also suggested that male adolescents who are involved with public service systems are at high risk for developing and maintaining multiple-substance use in adolescence.
Conclusions: Experience of childhood maltreatment is associated with problematic patterns of adolescent substance use and may shape the longitudinal course of substance use during 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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LONG-TERM COCAINE SELF-ADMINISTRATION BY RHESUS MONKEYS RESULTS IN INCREASED EXPRESSION OF α1 SUBUNITS OF THE GABAA RECEPTOR.

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Aims: We have shown previously that rhesus monkeys trained to self-administer cocaine under limited access conditions for 100 days show tolerance to the locomotor effects of the drug and escalation in cocaine taking. The present study is part of a series of experiments evaluating neuroadaptations in monkeys exposed to long-term limited access cocaine self-administration. The present study examined α1GABAA receptor immunoreactivity in reward-related nuclei(nucleus accumbens,NAc; anterior cingulate cortex,ACC; caudate,Cd; and putamen,Put)after long term cocaine self-administration.
Methods: Six male rhesus monkeys either self-administered cocaine intravenously or received passive infusions of saline yoked to the cocaine injections(yoked control) during 1 hour sessions for 100 days. Twenty-four hours after the last session, animals were sacrificed and their brains removed. The tissues were sectioned and immunohistochemistry(IHC) was conducted using a commercially available primary monoclonal antibody to the α1 subunit of the α1GABAA receptor.
Results: IHC results showed significantly higher immunoreactivity in the ACC and Cd, while no clear effect was found in the NAc and Put.
Conclusions: Many imaging studies have implicated the ACC as an area of increased activation following long-term cocaine exposure, and our results suggest neuroadaptations occur that compensate for this activation,i.e. a possible increase in inhibitory GABAergic signal. Previous research also shows increases in α1GABAA receptors in the VTA after cocaine exposure; however we saw no consistent corresponding increase in the NAc. The lack of change in the NAc and Put may be a result of compensation in the nuclei projecting to these regions,i.e. the VTA and cortical regions. Although further studies are needed to understand the relationship between the behavioral and molecular changes, our findings establish that neuroadaptations involving α1GABAA receptors occur as a result of chronic cocaine self-administration.
Financial Support: DA21420,DA11792,RR00168

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THE IMPACT OF COCAINE VACCINE (TA-CD) ON OPIATE USE IN METHADONE-MAINTAINED, OPIATE- AND COCAINE-DEPENDENT PARTICIPANTS.

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Aims: High rates of nonprescription opioid abuse among methadone-maintained participants have been observed. Identification of therapeutic options that would assist in further reduction of illicit opiate use are needed. This post-hoc analysis of a randomized clinical trial (Martell et al., 2009) is to examine the impact of the cocaine vaccine, TA-CD, on the use of other opiates (methadone excluded) in this sample. We hypothesized that participants who receive TA-CD and mount a high antibody response would display significantly fewer opiate positive (methadone excluded) urine toxicology results.
Methods: Post-hoc analysis of toxicology results over a 20 week period from participants enrolled in a methadone-maintenance treatment program with both opiate- and cocaine-dependence (N = 110) were examined via post-hoc univariate analysis of variance.
Results: The sub-group mounting a high antibody response (n = 21) demonstrated a higher percentage of opiate negative urines (79.7%) than the low antibody response sub-group (67.8%); however, this difference between groups was not statistically significant ($p = 0.110$). Overall, females were more likely than males to abstain from opiates during the follow up period ($p < 0.002$).
Conclusions: Contrary to expectations, antibody response sub-groups did not exhibit statistically significant opiate toxicology results. However, the higher percentage of opiate-negative urines in the high antibody response group warrants further investigation with larger samples.
Financial Support: Supported by NIDA R01-DA15477 (PI: Kosten)

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THE RELATIONSHIP BETWEEN OBJECTIVE AND SUBJECTIVE EFFECTS MEASURES USED IN ABUSE LIABILITY TESTING: AN EXPLORATORY ANALYSIS USING OPIOID AGONISTS.

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Aims: Multiple measures of subjective and objective drug effects are administered in the abuse liability assessment of drugs; however, the relationship between these measures has not been fully characterized. The current exploratory analysis focused on subjective measures of positive (e.g., visual analog scales [VAS] of drug liking, high) and sedative (e.g., sleepy VAS) drug effects, and pupil diameter, a commonly used physiological marker of opioid effects. The relationship between plasma drug concentration and effect was also evaluated.
Methods: Pharmacodynamic and pharmacokinetic assessments were conducted at specified time points following oral administration of oxycodone 60 mg, hydrocodone 60 mg, and morphine 120 mg in recreational drug users with moderate opioid experience (n= 28, 28 and 23, respectively). Various statistical approaches were taken to explore the relationship between each measure type, including Pearson correlations.
Results: Time to peak opioid effect was generally longer for pupil diameter compared to subjective measures, yet correlations between 'at the moment' subjective effects and pupil diameter over time for oxycodone and hydrocodone were significant, as were those with plasma concentrations ($r=0.3$-0.6, $p<0.05$). The relationship between pupil diameter and plasma concentrations of oxycodone and hydrocodone was also statistically significant ($r=0.3$-0.7, $p<0.001$). The relationship between plasma concentrations, subjective and objective effects was more modest for morphine, with correlations generally <0.4.
Conclusions: Although the time course of effects may differ, the current results indicate subject self-reports show a moderate to good relationship with a physiological measure of opioid effects.
Financial Support: This work was supported by Kendle Early Stage, Toronto.

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GROWING MOTIVATIONAL INTERVIEWING CAPACITY AND SUSTAINABILITY FROM A PARTNERSHIP STARTER PROJECT.

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Aims: Examine technology transfer strategies leading to the successful implementation of motivational interviewing (MI) by a large, private non-profit substance abuse treatment provider.
Methods: The Mid-Atlantic Addiction Technology Transfer Center assisted the Prince William County Community Services Board (PWCCSB) adopt MI in a substance abuse treatment program located in Manassas, Virginia through a structured series of dissemination activities including online instruction, face-to-face workshops, audio-taping, and performance feedback.
Results: Evaluation of the implementation-related events found that most Prince William County treatment staff were extremely to very satisfied with the training activities, including the taping and performance feedback process. A comparison of client outcomes following implementation of MI revealed a decrease in Adult Detention Center recidivism rates from the previous 10 year average of 32% to 26% in 2009 and 25% in 2010. Likewise, there was an increase in treatment retention rates between 2005 and 2007 of 2.7% after six visits and 2.3% after 12 visits.
Conclusions: Barriers to implementation were identified and used by management staff to create activities that supported implementation and decreased road blocks. Lessons learned from PWCCSB's implementation of MI include the importance of using a variety of strategies and the significance of management staff reinforcing counselors' use of MI by decreasing environmental and staff-related barriers, providing incentives, and creating an in-house resource for MI. This presentation will report on the specific approaches that enhanced the adoption process and highlight the management strategies created and used by PWCCSB to support and enhance the implementation and sustainability of MI.
Financial Support: Funded by the Mid-Atlantic ATTC SAMHSA/CSAT grant # 5UD1TI013415-09

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EFFECTS OF BUPRENORPHINE TAPERING SCHEDULE ON COCAINE USE AMONG OPIOID-DEPENDENT TREATMENT-SEEKERS.

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Aims: Buprenorphine is a partial u-opioid agonist with k antagonist properties approved by the FDA as a pharmacotherapy for opioid dependence. Human and animal studies with buprenorphine treatment demonstrate a significant reduction of opioid use, especially with poly-substance use. The aim of this study was to examine the potential differential effects of the two tapering schedules on cocaine use among subjects reporting concurrent cocaine use at baseline.
Methods: Sponsored by Clinical Trials Network (National Institute on Drug Abuse), this multi-site study compared two taper conditions, 7 days and 28 days, using buprenorphine for opiate use treatment. The intervention included a non-blinded dosing with Suboxone during the month stabilization phase. The primary treatment outcome reported no advantage in prolonging the duration of taper using buprenorphine for opioid dependence.
Results: Inclusion criteria for the secondary analysis was self-reported (ASI) cocaine use in the 30 days prior to treatment enrollment. At baseline, the 7-day taper group (n=104) reported an average 7.48 days (SD=8.4) of cocaine use and the 28-day taper group (n=129) reported 6.84 days (SD=8.4) within the previous month. During the treatment period, there were no significant differences between groups in their self-reported cocaine use days ($F=.58$; $p=.45$). However, at follow-up (3-month), the group randomized to the 7-day tapering condition reported significantly fewer cocaine use days compared to the 28-day tapering condition ($F=3.8$; $p\leq.05$).
Conclusions: The study suggests that buprenorphine may decrease cocaine use among treatment-seeking, opioid dependent individuals. Though the underlying interactions between buprenorphine and cocaine are not fully understood, a reduction of stimulant use benefits cocaine treatment research. Limitations of the current study include reliance on self-report measures of illicit substance use and reduced sample size over the course of treatment. Future research may question the neurological processes of using buprenorphine with cocaine users and developing appropriate treatment measures.
Financial Support: NIDA-CTN

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SEX DIFFERENCES IN RESPONSE TO GABOXADOL MODIFICATION OF COCAINE-INDUCED BEHAVIORS.

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Aims: The behavioral effects of repeated cocaine administration can be diminished by increasing GABA activity through inhibition of GABA uptake or administration of GABA analogs (Filip et al, 2006). We recently found that subcutaneous administration of Gaboxadol (GBX), a GABAA agonist selective for the α4βδ receptor, dampened the expression of cocaine-induced locomotion and stereotypy in a sexually dimorphic way. While GBX significantly decreased cocaine-stimulated locomotor activity in both male and female rats, it dampened stereotypy only in females. We hypothesized that cocaine pre-treatment induced a greater upregulation of α4βδ receptors in female rats compared to males.
Methods: We performed intracranial injections of GBX into the Nucleus Accumbens (NAC) to determine if activation of α4βδ receptors in the NAC could reproduce the effects of the previous experiment. Rats were surgically implanted with bilateral guide cannulae and recovered for 1 week. Then they received daily injections of cocaine (15 mg/kg ip) or saline followed by a 7-day withdrawal period. On the last day of withdrawal, rats were placed into Accuscan activity monitors and given 15 min to habituate; they were then given a bilateral infusion of 1 uM, 1 mM GBX or vehicle (saline) delivered over 5 min in a volume of 1.0 µL targeting the NAC. Behavioral measures (locomotor activity and stereotyped behaviors) were recorded for another 40 min.
Results: In cocaine pre-treated female rats, 1 uM GBX significantly increased and 1 mM GBX significantly decreased cocaine-stimulated locomotor activity compared to saline. In saline pre-treated females, 1 mM GBX significantly dampened cocaine-stimulated locomotor activity. In both male and female rats pre-treated with cocaine, 1 uM GBX increased and 1 mM GBX significantly decreased cocaine-stimulated stereotypic behaviors.
Conclusions: These data suggest that activation of GABAARs containing δ and γ subunits in the NAC contributes significantly to sex differences in response to cocaine sensitization.
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TREATMENT OF MDMA(ECSTASY)-ASSOCIATED HYPONATREMIA (MDMA-AH).

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Aims: To understand hyponatremia associated with 3,4-methylenedioxymethamphetamine 'ecstasy' (MDMA-AH) as a potentially life threatening disorder.
Methods: MEDLINE search identified 52 peer-reviewed publications on the prevalence, morbidity and mortality of (MDMA-AH) including over 20 fatalities from 12 countries.
Results: Hyponatremia [serum sodium concentration ([Na+]) < 135 mEq/L] may be life-threatening especially in previously healthy young female attendees at raves. The majority of cases are minimally symptomatic with restlessness, agitation, and disorientation which may rapidly progress to seizures, coma and death as seen in marathon runners with exercise-associated hyponatremia (EAH). Acute water intoxication occurs when avid fluid intake exceeds total losses.The proximate underlying pathophysiology is an inappropriate antidiuresis, as MDMA is a known secretogogue for arginine vasopressin (AVP)together with release of interleukin(IL)-6 from injured skeletal muscle during prolonged dancing. The inability to suppress AVP leads to acute water intoxication, fulfilling the diagnostic criteria for the syndrome of inappropriate antidiuretic hormone secretion(SIADH. Understanding this clinical paradigm dictates the emergent use of intravenous 3% saline to reduce acute cerebral edema. This evidence-based treatment has been shown to be safe as in EAH and is not associated with risk for demyelination syndrome as a complication of over rapid correction of chronic hyponatremia. In contrast, continued intake of oral hyptonic fluids or infusion of intravenous normal saline may exacerbate fluid overload with progression of neurological symptoms to respiratory arrest. AVP-receptor antagonists as novel aquaretic agents deserve study for treating mild to moderate cases.
Conclusions: The image of 'ecstasy' as a safe party drug is spurious. MDMA-AH in attendees at raves may be life-threatening due to acute cerebral edema as in previously healthy marathon runners during races. Understanding MDMA-AH as acute water intoxication due in part to inappropriate antidiuresis dictates the evidence-based use of intravenous hypertonic saline as the emergent treatment of choice.
Financial Support: not applicable

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INVESTIGATING A GENETIC MARKER OF VULNERABILITY FOR STIMULANT ABUSE.

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Aims: Individuals vary widely in their response to psychomotor stimulants and these differences may be associated with risk for developing abuse of these drugs. A growing literature suggests that sensitivity to stimulant reinforcement is influenced by genetic factors, with a greater prevalence of the D2 dopamine receptor (DRD2) A1 allele found among stimulant abusers than controls. What has not been examined to our knowledge is how individuals, prospectively identified as A1 carriers or noncarriers, may respond to stimulant subjective and reinforcing effects. We are examining whether DRD2 A1 allele carriers and noncarriers differ in their subjective and behavioral response to d-amphetamine (d-AMPH).
Methods: Healthy volunteers (30 allele carriers and 30 noncarriers) complete 36 double-blind sessions in which they repeatedly sample and choose between d-AMPH (5, 10 and 20 mg/70 kg) or placebo.
Results: Our data thus far suggest several exciting findings. First, A1 carriers and noncarriers (N=24) significantly differ on 16 of the 25 subjective effects items, with carriers reporting greater positive effects of d-AMPH than noncarriers (e.g., Liking, Good Effects, Elated, Overjoyed, Arousing/Stimulating Effects). Second, carriers generally demonstrate greater preference for d-AMPH over placebo than noncarriers. For example, carriers are choosing d-AMPH over placebo more often overall than noncarriers (81% vs. 61% of occasions, respectively) and demonstrating significant d-AMPH preference (i.e., at least 10 of 12 choices) twice as often than noncarriers (50% vs. 23%, respectively). We can also begin to examine how overall allelic prevalence may vary as a function of sensitivity to drug reinforcement. When we collapse subjects across allele status and place them into 1 of 5 categories based on d-AMPH choice (0%, 25%, 50%, 75% or 100% d-AMPH choice), there is a linear relationship between percentage of d-AMPH choices and percentage of individuals with the A1 allele.
Conclusions: These data provide the first experimental, prospective evidence that stimulant reinforcement may vary as a function of DRD2 allele status.
Financial Support: NIDA R03 DA027480.

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DOPAMINERGIC REGULATION OF RISKY DECISION-MAKING.

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Aims: Drug addiction is strongly associated with abnormal risky decision-making as well as alterations in dopamine receptor expression. Determining the involvement of specific brain regions and dopamine receptor subtypes in risky decision-making could provide information about the neurobiological underpinnings of drug addiction and other disorders associated with abnormal risk-taking. We tested the effects of drugs specific to D1-like and D2 –like receptors on risky decision-making in rats. Then, to determine if risk preference is related to dopamine receptor expression, in situ hybridization was used to quantify region-specific D1 and D2 receptor mRNA in rats characterized in risky decision-making.
Methods: During the "Risky Decision-making Task", rats were given choices between a small reward and a large reward associated with risk of punishment. To investigate how dopamine receptor activation modulates risk preference, we administered selective D1-like and D2-like receptor agonists and antagonists prior to task performance. Then, we examined the relationship between risky decision-making and baseline mRNA abundance of D1 and D2 receptors in drug naive rats using in situ hybridization.
Results: Agonists and antagonists specific to D1-like receptors had no effects on risky choice; however, the D2-like agonist bromocriptine reduced risky choice. D1 mRNA abundance in nucleus accumbens shell and insular cortex were both positive predictors of baseline risk preference, while D2 mRNA abundance in orbitofrontal cortex and medial prefrontal cortex predicted risky decision-making behavior in nonlinear fashion. Additionally, increased levels of D2 mRNA in dorsal striatum were observed in risk-averse rats in comparison to risk-taking rats.
Conclusions: Risky decision-making can be directly affected (reduced) by acute D2-like receptor activation, but trait risky decision-making appears to be a function of distinct patterns of both D1 and D2 receptor mRNA expression in various frontostriatal regions.
Financial Support: DA0233312 (NWS) & DA024671 (BS)

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ARMODAFINIL AND OTHER COGNITIVE ENHANCERS INCREASE EXTRACELLULAR NOREPINEPHRINE AND DOPAMINE IN RAT PREFRONTAL CORTEX.

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Aims: Armodafinil is a wake-promoting medication with cognitive-enhancing properties. The mechanisms underlying armodafinil's cognitive actions are not known but likely involve cortical circuits. Here we employed in vivo microdialysis to evaluate the effects of armodafinil and other known cognitive enhancers on extracellular concentrations of norepinephrine (NE) and dopamine (DA) in rat prefrontal cortex.
Methods: Anesthetized male rats were surgically prepared with jugular catheters and intracranial cannulae aimed at the prefrontal cortex. One week later, microdialysis testing was carried out in chambers equipped with photobeams to assess motor parameters. Armodafinil (5 & 15 mg/kg), methylphenidate (0.3 & 1.0 mg/kg), (+)-amphetamine (0.1 & 0.3 mg/kg) and phentermine (0.3 & 1.0 mg/kg) were administered via i.v. catheter. Extracellular levels of NE and DA were determined by HPLC-ECD.
Results: At the doses administered, armodafinil and other drugs caused simultaneous dose-related elevations in extracellular NE and DA. Interestingly, all drugs increased cortical catecholamines at doses that did not significantly increase forward locomotion. Methylphenidate, (+)-amphetamine and phentermine tended to increase NE more than DA, while armodafinil had the opposite profile of effects.
Conclusions: Our data show that armodafinil and other cognitive enhancers produce concurrent increases in extracellular levels of NE and DA in rat prefrontal cortex, suggesting a common mechanism for these agents. Moreover, the results agree with the hypothesis that stimulant-like medications recruit cortical substrates at doses below those required to elicit locomotor effects.
Financial Support: Generously supported by NIDA, IRP.

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GHB IN ADOLESCENT RAT INHIBITS CONTEXTUAL FEAR CONDITIONING.

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Aims: Our laboratory has previously shown using the Morris water maze that GHB causes deficits in spatial learning and memory in adolescent rats. The present study was undertaken to expand this finding by investigating the effects of acute and repeated administrations of GHB on contextual and cued fear conditioning in adolescent rats.
Methods: Groups of adolescent rats received either acute or repeated injections of one of two doses of GHB or saline either before training or testing. Rats were presented with a continuous tone for 30 s, at the end of which it received an electric shock delivered through the floor grid. Each animal's freezing behavior was scored.
Results: When injected prior to conditioning, both acute and repeated GHB significantly reduced the amount of freezing to the context in a dose-dependent manner. GHB did not significantly alter the amount of freezing elicited by the tone CS when injected either prior to conditioning or prior to testing.
Conclusions: In adolescent rats, acute GHB exposure impaired the acquisition of contextual fear memory but not the expression of previously conditioned responses to the context. GHB did not affect the acquisition or expression of auditory cued fear responses. Consistent with the findings of the acute administration experiment, repeated treatment with GHB disrupted the acquisition of contextual fear memory but not that of auditory cued fear memory in adolescent rats.
Financial Support: PHS Grant DA 018234

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SOCIALLY-ROOTED RESILIENCE AMONG IDUS: THE PROTECTIVE FACTORS THAT MAY HELP LONG-TERM IDUS REMAIN HIV UNINFECTED AND HELP OTHER INJECTORS STAY SAFE.

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Aims: Resilience has been shown to be related to positive health outcomes in general. We examine its relation to IDUs' engaging in safer injection practices.
Methods: An innovative intervention (Staying Safe) was developed based on strategies and practices of long term IDUs who have managed to remain HIV and HCV seronegative. A baseline 185-item survey was administered to 50 IDUs (29 male, 21 female) recruited initially from a needle exchange program and referrals from participants.
Results: Resilience characteristics (planning ahead, health communication, and external support) were correlated with safe practices such as storing sterile syringes, which reduces the risk of sharing needles.
Planning ahead: The majority of the participants answered "Often" and "Very Often" to a set of planning ahead questions, an indicator of ability to engage in strategies to stay uninfected. Planning to avoid drug withdrawal is correlated with storing sterile syringes ($r = .309$; $p = 0.035$), as is planning to have steady access to sterile syringes to storing sterile syringes ($r = .502$; $p = .001$).
Health communication: 68% of participants reported that they discussed with other injectors the need to take drugs safely, which was correlated with storing sterile syringes ($r=.326$, $p=.025$)and the number of times of their providing the following to others: sterile syringes ($r = .837$, $p=.000$), clean cotton ($r=.839$, $p=.000$), and clean cookers ($r=.855$, $p=.000$).
External support: 85% of participants indicated that they had one or more good relationships with non drug users. This was correlated with storing sterile syringes ($r=.446$, $p=.002$) and reduced drug intake on their own ($r=.308$, $p=.035$).
Conclusions: Despite major risks in the lives of long-term IDUs, many try to prevent themselves and others from getting infected with HIV/HCV. Resilience factors should be further studied as key aspects in the HIV/HCV prevention/intervention for IDUs.
Financial Support: NIDA grant # T32-DA007233-27

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ISSUES OF DIVERSITY IN WORKFORCE DEVELOPMENT.

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Aims: To better understand the extent of the substance abuse workforce's need to understand the cultural needs of their clients as they related to interventions for substance use disorders.
Methods: Sample: 30 substance abuse counselors from IA, MN, SD, and WI participated in interviews: 66.5% females and 33.5% males; 86% Caucasian and 14% African American, Native American, or Hispanic/Latino.
Procedure: Substance abuse counselors were recruited from Prairielands ATTC state advisory boards. Each participant was given a telephonic qualitative interview with questions related to demographics, understanding and value of cultural competence, training on working with diverse clients, and plausibility of systemic change to improve services to diverse clients.
Results: Qualitative analysis indicated that providers from urban and rural areas had different needs for technical assistance and training. Urban providers indicated a need for more knowledge about African-Americans; and implications of low income, segregated communities, and gang membership. Rural providers indicated that their training needs were specifically focused on cultural issues in Native American (NA) and LGBT clients. Compounding rural providers' need was the diversity of clientele due in part to state immigration patterns. Both rural and urban providers felt a need for technical assistance (TA) and training in how to support and treat the newly poor and how to address loss of status, job, home, etc.
Conclusions: Perceived training and TA needs differed in counselors from urban and rural areas. Rural providers expressed a need for cultural sensitivity training in new areas because of rapidly changing demographics in these areas.
Financial Support: Substance Abuse and Mental Health Services Administration/Center for Substance Abuse Treatment

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AN EXAMINATION OF PREDICTORS OF FAMILY AND INDIVIDUAL TREATMENT ATTENDANCE AMONG SUBSTANCE-ABUSING ADOLESCENT RUNAWAYS.

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Aims: Runaway adolescents report high rates of family and individual problems, and are considered difficult to engage and maintain in substance abuse treatment. This study compared predictors of session attendance for family and individual therapy modalities with the goal to improve treatment retention and ultimately, treatment outcomes.

Methods: Participants were recruited from the only runaway shelter in Columbus, Ohio. Eligible participants (N=179) were between the ages of 12 to 17 years, and met DSM-IV criteria for alcohol or drug abuse or dependence. Upon completion of the baseline assessment, adolescents were randomly assigned to one of three treatments: (1) Motivational Enhancement Therapy (MET) (n = 61), (2) the Community Reinforcement Approach (CRA) (n = 61), or (3) Ecologically-Based Family Therapy (EBFT) (n = 57).

Results: Hierarchical linear regression was used to predict the proportion of sessions attended for each treatment condition for those who attended at least one therapy session. Family factors accounted for 25.4% additional variance in EBFT attendance. Adolescents who were Black/African American and who reported higher levels of parental monitoring attended CRA sessions more frequently than other adolescents. Younger adolescents attended MET sessions more frequently than older adolescents and higher levels of task oriented coping strategies were significantly associated with higher MET attendance rates.

Conclusions: This study's findings suggest that individual and family factors predict therapy attendance but these factors differ depending upon the treatment modality. The lack of similarity in predictors of attendance provides some support for investigating matching treatments to baseline client characteristics. If the most appropriate treatment is offered, adolescents may be more likely to attend sessions which might ultimately lead to better treatment outcomes.

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A PROGRAMMATIC TREATMENT ENGAGEMENT INTERVENTION FOR HOMELESS VETERANS WITH CO-OCCURRING MENTAL HEALTH AND SUBSTANCE ABUSE PROBLEMS.

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Aims: The current study evaluated a low intensity programmatic treatment engagement intervention to assist homeless Veterans transitioning from residential care into the community.

Methods: Homeless Veterans (n=363) were recruited from the Domiciliary for Homeless Veterans Residential Care Program. Veterans either received treatment as usual (TAU; n=121) or TAU along with Maintaining Independence and Sobriety Through Systems Integration, Outreach, and Networking (MISSION; n=242), which is a low intensity programmatic treatment engagement intervention. Group assignment was based on the availability of MISSION treatment slots during informed consent.

Results: While Veterans receiving either TAU or TAU along with MISSION both showed improvement, the largest differences were noted in the reduction of hospitalization days (20% vs. 43%), drinking to intoxication (26% vs. 42%), and ability to control violent behavior (25% vs. 47%) between TAU and TAU with MISSION groups. Veterans receiving TAU along with MISSION showed the largest improvements. Additional findings related to addiction and services will also be reported.

Conclusions: Results indicated that the one year low intensity MISSION program, augmenting treatment as usual, can improve treatment engagement and behavioral outcomes. The authors have completed a treatment manual to implement the MISSION program which offers rapid housing placement in conjuction with case management services provided by the VA.

Financial Support: MISSION was supported by Grant # TI16576 funded by the Substance Abuse and Mental Health Services Administration (SAMHSA).

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AN INDIRECT SELF-REPORT SCREENER FOR IDENTIFICATION OF DRUG USE IN PREGNANT WOMEN.

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Aims: Most drug use screening measures rely on and are validated against self-report. Fear of negative consequences often promotes denial of drug use. For pregnant women, social stigma and fear of legal consequences make underreporting of drug use even more likely. An indirect screener that could effectively identify pregnant women at risk for illicit drug use without reliance on disclosure would be clinically significant. The purpose of the current study was to develop and validate an indirect measure of prenatal drug use by comparing correlates of prenatal drug use to urinalysis results.

Methods: Pregnant women attending an urban OB clinic were recruited and consented to participate in a two-phase study. In Phase 1, women completed a 20-min computerized assessment which included a true/false index of 74 items known to tap correlates of drug abuse and dependence. Subsequently, in Phase 2, participants were asked to provide a urine sample for drug testing. Women received a $20 gift card after they participated in each phase ($40 max).

Results: To date, 97 women have completed Phases 1 and 2 (94% completion rate). Participants were primarily African-American (69%), single (79%), and receiving public assistance (73%). Preliminary analyses found 23 of 74 items yielded significant zero-order correlations with the criterion (i.e., urinalysis positive for any drug use). Further item reduction based on content and logistic regression analyses reduced the list to 5 items, which when summed resulted in a screener with sensitivity = .83, specificity = .73, and AUC = .82. Upon study completion, cross-validation within the larger sample will be of paramount importance.

Conclusions: Preliminary findings appear promising for development of a sensitive indirect prenatal drug use screener. Such a measure could be a useful tool for identifying at-risk women in OB-clinics and similar settings, where time and resources are limited.

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TRAINING SUBSTANCE ABUSE CLINICIANS IN MI USING TELECONFERENCING SUPERVISION.

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Aims: Evaluate supervision methods used to increase MI skill in community based substance abuse clinicians following completion of a 2-day MI workshop.

Methods: 100 community based substance abuse clinicians were randomly assigned to one of three supervision conditions (teleconferencing, tape review, or workshop only) following a 2-day MI workshop. Post-workshop supervision was based on 5 practice sessions with actors conducted at participating treatment clinics. Teleconferencing supervision (TCS) provided real time feedback and modeling from a remote supervisor. Tape review (TAPE) provided delayed feedback on tape recorded sessions. Workshop only (TAU) did not provide supervision. Clinician MI skill was assessed at four time points: preworkshop, and 1, 8, and 20 weeks post workshop. Mixed effect linear models using a GEE analytical framework were used to assess the effects of supervision condition on MI skills over time.

Results: TCS was superior to TAPE on measures of clinician empathy ($z=3.21$, $p < .002$) and MI spirit ($z=2.48$; $p < .02$). TCS was superior to TAU on measures of counselor empathy ($z=3.21$, $p < .002$), MI spirit ($z=2.48$; $p < .02$), and MI non-adherent behaviors ($z=-2.3$; $p < .03$). For all MI skill measures, clinician skill level prior to post-workshop training was significantly related to MI skill level following post-workshop supervision.

Conclusions: All clinicians increased MI skill after workshop attendance. However, those receiving supervision continued to improve. TCS produced greater gains in MI Spirit and Empathy and reduced MI non-adherent statements. The data replicate previous findings suggesting workshop training alone is inadequate for promoting the long term acquisition of counseling skills. TCS offers a remote supervision system that can facilitate and maintain the acquisition of counseling behaviors following participation in a traditional workshop.

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AEROBIC EXERCISE DECREASES THE ACQUISITION OF COCAINE SELF-ADMINISTRATION.

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Aims: Aerobic exercise decreases cocaine self-administration in laboratory animals and is associated with positive outcomes in substance abuse treatment programs; however, less is known about its efficacy in preventing the establishment of regular patterns of substance use in drug-naive individuals. This latter point is particularly important from a public health standpoint because a rapid transition from initial drug exposure to regular patterns of drug use is a reliable predictor of whether an individual will develop problems with substance abuse and dependence. The purpose of the present study was to examine the effects of aerobic exercise on the acquisition of cocaine self-administration in young adult male rats.
Methods: Male, Long-Evans rats were obtained at weaning (21 days) and assigned to sedentary or exercising conditions immediately upon arrival. After six weeks, rats were surgically implanted with intravenous catheters and allowed to recover for three days. Following recovery, rats were placed in operant conditioning chambers for 2 hours/day for 15 consecutive days. Each session began with a noncontingent priming infusion of cocaine, followed by a free-operant period in which each response on the active lever produced an infusion of cocaine on a fixed ratio (FR1) schedule of reinforcement. For days 1-5, responding was reinforced with 0.25 mg/kg/infusion cocaine; for days 6-15, responding was reinforced with 0.75 mg/kg/infusion cocaine. In addition, all rats were food-deprived to 90% of their free-feeding body weight during days 11-15.
Results: Sedentary rats acquired cocaine self-administration at a significantly faster rate, emitted a significantly greater number of active lever presses, and had significantly higher rates of cocaine intake than exercising rats.
Conclusions: These data indicate that aerobic exercise decreases the acquisition of cocaine self-administration and may be an effective intervention in substance abuse prevention programs.
Financial Support: This study was supported by the National Institutes of Health (NIDA Grant DA027485 to MAS).

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PEER-LED INTEGRATION OF MOTIVATIONAL INTERVIEWING INTO COMMUNITY CORRECTIONS.

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Aims: We sought to facilitate the integration of Motivational Interviewing (MI) into a community corrections agency providing pretrial, probation, Reentry, Drug Court and Restorative Justice services for offenders, 70% with drug-related offenses, by coaching peer leaders to train groups of staff in MI.
Methods: Agency staff members receive training in communication skills upon hiring. Some receive further training in MI, selected as an EBP for drug use and other criminogenic factors in 2005. During 2009-2010, 6 peer leaders worked with an MI trainer to develop their skills in training MI. The group met monthly for 90 minutes to review topics drawn from eight stages of learning MI, with demonstrations of training the specific MI construct. Peer leaders then trained a group of staff members each subsequent month. After a year, the peer leaders taped practice samples that were rated using the Motivational Interviewing Treatment Integrity (MITI) code. They shared their tapes and ratings with their small groups to encourage staff members to record practice samples.
Results: Peer leaders trained 7-8 staff in small groups in co-trainer pairs monthly. Two left the agency and 1 was replaced with an experienced MI practitioner during the year. Peer leaders obtained high scores on the MITI indicating excellent MI fidelity. Peer leaders reported frustration with a lack of application of MI skills by staff. Staff members are recording their sessions and will receive feedback to improve skills. Future performance evaluations will include MI skills assessment.
Conclusions: Building capacity within an agency's own staff is one way to integrate an evidence-based practice into a community corrections. While the peer leaders demonstrated strong fidelity to MI in rated samples, they noted variability among line staff in interest and enthusiasm for MI and in their capacity to integrate it into everyday work with drug abusers and other offenders in the criminal justice system.
Financial Support: Jefferson Area Community Corrections and NIAAA R01 AA015930

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GENDER DIFFERENCES IN RISK FACTORS FOR NEW-ONSET NONMEDICAL USE OF OPIOIDS, HEROIN AND OTHER DRUGS: FINDINGS FROM NESARC.

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Aims: The abuse of opiate-derived drugs leads to substantial morbidity and mortality; thus, it is important to explore risk factors for these behaviors, as well as differences between genders in these risk factors. This study used a nationally representative sample of U.S. adults to examine gender, other demographics, substance use, psychopathology, bodily pain, and stressful life events as risk factors for new-onset opioid use in comparison with new-onset heroin use, new-onset marijuana use only, new-onset other drug use, continuing drug use, and no drug use. Gender was examined as a moderator of these risk factors.
Methods: Data were analyzed from waves 1 and 2 of the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC), conducted from 2001-2002(N=43,093) and 2004-2005 (N=34,653), respectively. Unadjusted differences were examined using descriptive statistics, chi-square tests, and ANOVA. Adjusted effects and moderation were examined using multinomial logistic regression.
Results: Females were more likely to be new-onset heroin users relative to new-onset opioid users, while males were more likely to be new-onset opioid users relative to continuing drug users. Bodily pain, problem drinking, binge drinking, and depression tended to be risk factors for new-onset opioid use relative to the other groups. Stressful life events predicted new-onset opioid use for women, but not for men. Problem drinking increased risk of new-onset heroin use for men only, and decreased risk of new-onset marijuana use for females only, relative to new-onset opioid use.
Conclusions: In conclusion, using data from a large nationally representative sample of U.S. adults this study found important differences in risk factors between new-onset users of different drugs, some of which differed by gender. These findings have important implications for intervention efforts.
Financial Support: Supported by AMBRF/The Foundation for Alcohol Research Grant awarded to Gregory G. Homish

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VERBAL AND VISUAL LEARNING AND MEMORY IN SHORT- AND LONG-TERM HEAVY CANNABIS USERS.

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Aims: The aim of this project was to determine the nature of memory deficits in cannabis users across the life span. We explored how varying durations of exposure to cannabis during adolescence and adulthood affects verbal and visuospatial learning and memory.
Methods: 40 long-term heavy cannabis users (aged 21-49 years), 40 matched controls (aged 19-55), and 21 short-term heavy cannabis users (aged 18-36 years), completed the California Verbal Learning Test (CVLT) and its visuospatial analogue, the Brown Location Test (BLT), to assess verbal and visuospatial learning and memory.
Results: Both cannabis groups performed worse on the immediate learning trial following interference and long-delay recall of the CVLT. Long-term heavy users also demonstrated deficits in learning over trials and recognition relative to controls. For the BLT, both groups were impaired in short- and long-delay recall and recognition and long-term users also demonstrated retroactive interference and loss after consolidation deficits relative to controls. In both cannabis groups, cumulative cannabis dose measures were negatively correlated with several CVLT trials and age of first cannabis use and duration of use measures were negatively correlated with several BLT trials.
Conclusions: Both cannabis groups demonstrated a similar pattern of deficits on both tasks relative to controls; however long-heavy cannabis users demonstrated a wider range of deficits and the pattern of deficits between tasks was different. Our findings suggest that cannabis may differentially affect brain regions subserving verbal and visuospatial memory, and that age of onset, duration and cumulative dose of exposure significantly affect cognitive performance.
Financial Support: The study was supported by a NHMRC project grant (I.D. 459111). M. Yücel is supported by a NHMRC Clinical Career Development Award (I.D. 509345).

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CONFIDENTIALITY AND INTEGRATION OF SUBSTANCE USE DISORDERS TREATMENT WITH MEDICAL CARE.

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Aims: The implementation of health care reform may usher in an era of increasing integration of treatments for substance use disorder (SUD) treatment with treatments of other health problems. While there are numerous benefits to coordinated care, a danger may lie in the decrease of confidentiality protections. This presentation summarizes reasons for confidentiality protections in SUD treatment, reviews the degree that protections may be threatened by recent developments, and makes suggestions for maintaining confidentiality while promoting coordination of care
Conclusions: Federal confidentiality regulations (42 CFR Part II) exist for treatment of SUD (both drugs and alcohol), providing more stringent protections than regulations for mental health or medical care. They were enacted in the 1970s, a time of independent SUD treatment programs, with the rationale that patients' attempts to overcome their addiction should not be held against them. They require patient consent for each disclosure (no blanket waivers of consent) and forbid re-disclosure by the recipient without patient consent. Several recent developments promote coordinated care, including the Mental Health Parity and Addiction Equity Act of 2008, increasing use of electronic medical records, and the health care reform legislation of 2010. These developments reflect a move toward integrating SUD treatment with mainstream medical care. Confidentiality dilemmas in this new environment include: Degree that patient privacy and confidentiality will be maintained, levels of permission or waiver that are acceptable for disclosure, whether to include dependence or SUD treatment in the medical record, and consequences of linked records for fiscal reimbursement and insurance coverage. We posit some provisional guidelines to maintaining confidentiality in a coordinated care environment. Research is needed on the degree to which these issues will become problematic in the field.
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RECENT DRUG BEHAVIORS AMONG A SAMPLE OF HIV-POSITIVE ADULTS IN MIAMI, FL.

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Aims: There are very few estimates of the prevalence of illegal drug use among individuals infected with the HIV virus. These data were collected as part of a larger study, and provide information on self-reported drug use behaviors among a sample of HIV positive adults.
Methods: Data was obtained and analyzed from a larger study, which aims to investigate the effect of drug use on HIV progression. 123 HIV positive adults were enrolled and demographic information, health history, drug use history, and medical records were obtained.
Results: Of a sample of 123 adults who have been infected with HIV, 40% (n= 49) reported to have used an illegal drug in the past 30 days. The drug using cohort was comprised predominantly of males (n = 38), then females (n= 10), followed by transgendered (n=1). African Americans represented the racial majority of drug users (n=32), and the sample as a whole (70%) followed by Caucasian (n=15). 16% of the drug using cohort identified themselves as Hispanic, compared to only 1% of the non-drug using sample. The majority of drug users reported using Crack/cocaine (59 %) in the past month, followed by marijuana (22%), and methamphetamine (12%). 6% of the sample reported using a combination of marijuana and cocaine within the past month, commonly referred to as "dirties."
Conclusions: These data indicate that among a sample of HIV positive adults, a substantial amount report recent drug use behaviors. Implications include substance abuse treatment efforts targeted towards individuals infected with HIV.
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YOUNG ADULTS WITH STIMULANT ABUSE: IMPULSIVITY AND BRAIN DYSFUNCTION.

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Aims: Stimulant abuse (SA) may have a serious effect on brain development and maturation in adolescents and young adults. Adults with this disorder show cognitive performance deficits and impulsivity. The first aim of this study was to examine impulsivity and cognitive impairments as well as neurobiological abnormalities in young adults recently abstinent from cocaine or stimulants as compared to matched controls. A second aim was to determine whether recovery from impairments occurred after 60 days of treatment and abstinence.
Methods: 18 recently abstinent (30 days) young adults in treatment for SA and 19 age, gender, and education matched controls underwent a battery of personality and impulsivity rating scales including: Barratt Impulsivity, EASI, and Behavioral Inhibition/Activation. They also completed computerized tasks measuring impulsivity and cognitive impairment: DPX, Delay Discounting (DD), Stop Signal; and brain imaging: fMRI with DTI and MRS. This battery was repeated 60 days later (T2).
Results: SA Subjects (12 males, 6 females, mean age 21.6) and 19 controls (14 males, 5 females) completed the tasks. SA subjects were more impulsive on all subscales of the Barratt ($p<.001$), and rated higher on fun seeking ($p<.05$) and punishment sensitivity ($p=.001$). On the DD task, group differences emerged with SA subjects (vs. controls)having preference for more immediate rewards ($p=.047$). Brain imaging revealed lowered cortical blood flow in the parietal, temporal and cingulate areas. At T2, impulsivity still persisted and was significantly greater than controls.
Conclusions: Youth with SA demonstrate significant impairments in impulsivity and reward delay measures. No improvement in impulsivity was seen at 60 days. Either recovery may require a longer period of time or this is an underlying trait. Perfusion deficits may indicate damage from stimulants/cocaine. Further analyses and research will study recovery or persistence of deficits.
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PATHWAYS TO PRESCRIPTION OPIOID ADDICTION.

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Aims: The pathways to prescription opioid addiction are likely more varied than for other substances of abuse due to the possibility of therapeutic exposure. The objective of this study was to determine the variety of pathways leading to addiction to pharmaceutical opioid products.
Methods: Adults with prescription opioid addiction were interviewed to retrospectively determine lifetime timelines related to prescription opioid use and addiction.
Results: A total of 327 interviews have been conducted. Preliminary results from 75 subjects (mean age 36 ± 9 years, 65% male) are available. First exposures were recreational for 45% (mean age 20 ± 6 years) and therapeutic for 55% (mean age 22 ± 8 years, ns). Most first therapeutic exposures involved codeine (42%) or oxycodone (37%). Most first recreational exposures involved hydromorphone (35%), oxycodone (32%) or morphine (21%). The source of opioid for first recreational exposure was from friends, either for free (47%) or purchased (24%). Following first therapeutic exposure, 68% continued using prescription opioids after their supply ran out. For the whole group, the transition period from use to self-identified problem with prescription opioids had a mean duration of 2.6 ± 3 years. During this period, significant stressors included family (38.7%), relationships (25%), low mood (17%), and bereavement (15%). Thirty percent endorsed taking the opioids to help cope and 56% indicated someone had expressed concern over their use during this period. The mean age when self-identified the problem was 27 ± 8 years; mean age first sought treatment was 30 ± 9 years.
Conclusions: Understanding the role of therapeutic exposures in the development of prescription opioid addiction and the phenomenology of the progression from prescription opioid use to addiction, is clinically very important. This will be the premise from which prevention and treatment approaches can emanate.
Financial Support: Health Canada

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PREDICTING RECIDIVISM FOR RELEASED STATE PRISON OFFENDERS: EXAMINING DRUG INVOLVEMENT AND RESIDENTIAL CLUSTERING EFFECTS ON THE LIKELIHOOD OF REINCARCERATION.

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Aims: To examine the influence of drug involvement and residential clustering of state prison ex-offenders on the likelihood of re-incarceration within 3 years of release.
Methods: De-identified administrative data on a sample of 5354 state prisoners released to Philadelphia between 2002 and 2006 were used to examine predictors of re-incarceration within 3 years of discharge. Data relating to each subject's address at sentencing was geocoded using Geographic Information Systems (GIS). Logistic regression modeling identified significant predictors of re-incarceration. Independent variables included demographic characteristics, drug involvement, and type of offense. The rate of re-incarceration within 3 years of all ex-offenders living within one mile of each individual releasee was also calculated as an indicator of residential clustering. Subjects living in areas with high rates of re-incarceration were expected to be more likely to be re-incarcerated themselves due to potential interactions with repeat offenders.
Results: Results indicate that the likelihood of re-incarceration is suppressed by being female (OR=0.70, p<.05)and being older (OR=.98, p<.001). Re-incarceration is more likely for African Americans (OR=1.20, p<.01), those committing a drug (OR=1.13, p<.08) or other kind of offense(OR=1.33, p<.001) as compared to a violent offense, and living nearby other ex-offenders who are re-incarcerated at a higher than average rate(OR=1.57, p<.001). After accounting for the influence of these other explanatory variables, drug involvement is found to increase the likelihood of re-incarceration (OR=1.39, p<.005).
Conclusions: Drug involvement and the proximity of living near other ex-offenders who become re-incarcerated increases the likelihood of recidivism. Re-entry programs need to particularly address substance abuse issues of ex-offenders as well as take into consideration the residential locations of their clients.
Financial Support: NIDA grant #1U01DA025284-01, S. Belenko, Principal Investigator

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EFFECTS OF ENVIRONMENTAL ENRICHMENT ON THE LOCOMOTOR STIMULANT EFFECTS OF REPEATED NICOTINE PRETREATMENT AND THE RELATIONSHIP WITH BRAIN NICOTINIC ACETYLCHOLINE RECEPTOR DENSITIES IN RATS.

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Aims: Rats raised in an enriched environment have a decreased sensitivity to the locomotor stimulant effects of nicotine. The purpose of the present study was to determine if environmental enrichment during development can alter sensitivity to the locomotor effects of repeated nicotine exposure and brain nACh receptor densities.
Methods: Male Sprague-Dawley rats were raised in either an enriched condition (EC) or an isolated condition (IC) under a 12/12 hr light/dark cycle, with lights on from 6:00-18:00 hr. EC and IC rats were injected for 14 days with either 0.3 mg/kg (s.c) nicotine or saline. On pretreatment days all animals were injected with either saline or nicotine (4-5/group) and placed directly into the locomotor chambers for 45 mins. Following completion of the 14 days of pretreatments brains were collected for autoradiography in order to determine nicotinic receptor density in various brain regions.
Results: Both EC and IC rats across sessions showed an increase in locomotor activity with repeated nicotine exposure. The within session analysis revealed that, both EC and IC rats exhibited a sensitization to the hyperactivity effect of acute nicotine and a tolerance to the hypoactive effect of acute nicotine. EC rats treated with nicotine exhibited a significant increase in locomotor behavior compared to their saline counterparts, whereas IC rats did not. [125I]Epibatidine binding in coronal sections suggests differences in nACh receptor density in mesolimbic regions from EC versus IC brains. Also, nicotine-induced locomotor behavior correlated with nACh receptor densities.
Conclusions: These results suggest that environmental enrichment alters the locomotor stimulant effect of nicotine by differentially regulating nACh receptor number.
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SOCIAL AND ENVIRONMENTAL ENRICHMENT ALTER THE EFFECTS OF MDMA ON COCAINE CONDITIONED PLACE PREFERENCE IN MALE ADOLESCENT RATS.

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Aims: MDMA (ecstasy) is used predominately by adolescents and young adults. Young MDMA users are more likely than non-users to use other drugs, including cocaine. The response to stimulant drugs can be affected by environmental factors, however there is very little information about the role that housing conditions play in mediating the effects of MDMA in adolescence. This study was done to investigate whether social and environmental conditions alter the effects of MDMA on cocaine conditioned place preference (CPP).
Methods: On postnatal day (PND) 23, rats were housed in one of several conditions. Both social (# of rats/cage) and environmental (availability of toys) factors were manipulated. Isolated rats were housed alone (1 rat/cage) in an environment that was impoverished with no toys (II) or enriched with toys (IE). Other rats were housed in groups of three with (SE3) or without (SI3) toys. Starting on PND 30, 5 mg/kg MDMA was injected IP once daily for 5 consecutive days. On PND 38, CPP began with a 30 min pretest. For the next 3 days, rats were trained with saline in the morning and cocaine (0, 1, 3, 5, 10, or 20 mg/kg) in the afternoon. On PND 42, rats were tested for 30 min to determine whether there was an increase in the amount of time spent in the cocaine-paired side.
Results: In rats without environmental enrichment (II and SI3), maximal CPP was increased after MDMA compared to saline. Environmental enrichment blocked this effect; however, there were shifts to the left of the dose-effect curves for cocaine CPP in both the IE and SE3 rats. Maximal CPP was observed in II rats to 10 mg/kg cocaine, in SI3 rats to 5 mg/kg cocaine, and in IE and SE3 rats to 3 mg/kg cocaine. Thus, after MDMA, the environmentally enriched rats exhibited a significant CPP to a lower dose of cocaine than impoverished rats, regardless of the social condition.
Conclusions: These findings show that MDMA increases cocaine reward in male adolescents, and environmental enrichment alters this effect.
Financial Support: NIDA grant DA023996

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TELEMEDICINE-BASED THERAPY FOR RURAL OFFENDERS WITH A HISTORY OF HAZARDOUS DRINKING.

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Aims: Many rural offenders have a history of hazardous alcohol use, yet few get formal treatment. This presentation includes the following aims: 1) To profile rural reentering offenders with a history of hazardous alcohol use before prison; 2) To examine preliminary alcohol outcomes of telemedicine-based therapy delivered in parole offices.
Methods: Baseline data was collected through face-to-face interviews with rural offenders under community supervision in two Kentucky districts. Participants were consented and screened using the AUDIT. Measures focused on alcohol and other drug use, criminal activity, and treatment history prior to prison. Participants were then randomly assigned to re-entry services as usual (n=32) or to telemedicine-based Motivational Enhancement Therapy (n=30) delivered via videoconferencing equipment in the rural parole office.
Results: Data collection is on-going (n=62). Preliminary findings indicate that participants' average AUDIT score was 24.0, average days drinking in a week was 3.7, and average number of drinks during an episode was 14.0 drinks. Despite this alcohol use pattern, only 27.4% reported ever being in alcohol treatment. In addition, 75.8% also reported other drug use before prison. Follow-up interviews conducted at 3 months post-baseline (82% of those eligible) indicate that participants in the MET condition reported significantly fewer days of alcohol use compared to the services as usual condition - 3.2 days vs. 12.9 days (t(33)=5.11, p<.05).
Conclusions: Findings suggest that a large number of re-entering rural offenders reported at-risk levels of alcohol use prior to prison and few had a history of formal treatment. These preliminary findings indicate that telemedicine may be a feasible option for delivering substance abuse interventions in real-world settings such as parole offices. Implications will be discussed with the goal of increasing access to effective treatment approaches for rural offenders in order to reduce risky alcohol use.
Financial Support: Project supported by NIH/NIAAA, R21-AA017937.

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THE DOPAMINE STABILIZER (-)-OSU6162 SELECTIVELY DECREASES VOLUNTARY ETHANOL CONSUMPTION IN RATS: IMPLICATIONS FOR A NOVEL TREATMENT OF ALCOHOL USE DISORDER.

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Aims: The dopamine (DA) system is a possible target for the treatment of alcohol use disorders (AUD). Alcohol's actions on the DA system are critical in mediating its acute reinforcing effects. Furthermore, a downregulated DA system during abstinence might lead to craving and relapse to drinking. Recently, clinical studies suggest that the partial D2 agonist aripiprazole, might be valuable in the treatment of AUD. "Dopamine stabilizers" is a new class of compounds, clinically tested for the treatment of schizophrenia and Huntington's disease, invented by Arvid Carlsson and coworkers at Gothenburg University. These compunds inhibit DA-ergic signaling when endogenous DA levels are high and enhance the signaling when DA levels are low. Thus, these compounds has similar effects as partial agonists, but the mechanism of action is not fully understood. Here, we are using an animal model to evaluating the potential of the DA stabilizer (-)-OSU6162 as a novel treatment of AUD.
Methods: Wistar rats were given access to 20% ethanol using a intermittent-access-2-bottle-choice model for at least 3 months prior to acute and long term OSU6162 treatment. The effects on ethanol intake, preference for ethanol and water intake was analysed.
Results: Acute and long-term OSU6162 treatment selectively decreased voluntary ethanol intake and preference without decreasing water intake in rats consuming high but not low amounts of ethanol.
Conclusions: The mechanism of action for OSU6162's ability to decrease ethanol intake is unknown. However, it is possible that OSU6162 normalize DA-signaling following long term intake of high amounts of ethanol and thereby modulates the rewarding effects of ethanol. These results are, to our knowledge, the first to indicate that the DA stabilizer OSU6162, may serve as a novel treatment of AUD.
Financial Support: The Swedish Research Council, Eva and Oscar Ahrén Research Foundation Stockholm, Socialstyrelsen Fonder, Karolinska Institutet Research Foundations and The Swedish Brain Foundation

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ASSOCIATIONS AMONG PAIN, SUBSTANCE USE AND DEPRESSION IN HIV-POSITIVE MEN.

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Aims: Investigation of correlates of pain in HIV, in addition to disease severity, has often noted co-occurrence of pain with illicit drug use and depressive symptoms. The complex nature of associations among clinical symptoms (e.g., CD4+ counts), demographics, pain, depressive affect, and drug use in HIV suggests testing mediated models that assess relations simultaneously.
Methods: Structural equation models using measures collected over 6 years tested a model in which pain mediated the relationship between clinical status (CD4+ count), demographics (education, ethnicity,age), and outcomes of depressive symptoms (CES-D), and illicit drug use (heroin, crack, marijuana) among 921 HIV+ gay/bisexual men from the Multicenter AIDS Cohort Study (MACS).
Results: Fit indexes in the predictive path model were excellent. A lower CD4+ count and less education significantly predicted more pain. Pain predicted more use of crack, heroin, and marijuana, and greater depressive symptoms. Furthermore, African-American ethnicity independently predicted more crack cocaine use and a younger age predicted more depressive symptoms.
Conclusions: Although illicit drug use may exacerbate HIV disease progression, clinicians should be aware that HIV+ individuals may be self-medicating to lessen the effects of pain in HIV. Furthermore, participation in a deviant subgroup where drugs are readily available may be more common among men who are HIV+, especially those of minority ethnicity. More targeting of drug abuse treatment and interventions toward these vulnerable groups is warranted as well as recognition of the need to provide effective and appropriate pain treatment for HIV+ individuals especially as the disease progresses.
Financial Support: MACS is funded by the National Institute of Allergy and Infectious Diseases, with additional funding from the National Cancer Institute; and the National Heart, Lung, and Blood Institute. Additional support was provided by the National Institute on Drug Abuse through 1R01-DA022936,P01-DA01070-37,and DA036093.

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A MEASURE OF THERAPEUTIC GROUP PROCESS FOR SUBSTANCE-ABUSING TEENS.

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Aims: Group-based substance abuse treatment is often delivered in youth correctional facilities, yet there is concern that groups may be iatrogenic. Few measures with demonstrated sound psychometric properties exist to track group behavior. Aim – To demonstrate adequate reliability and validity for the newly developed Group Process-Group Level measure (GP-GL) for teens, counselors and supervisors.
Methods: **N** = 175 teens (**M** = 16.9 years old, **SD** = 1.1) were randomized to 1 of 2 group-based substance abuse treatments, each lasting 10 sessions over 10 weeks. Within the sample 31% were White; 89% were boys; and 29% and 61% were alcohol and marijuana dependent, respectively. Supervisors rated 28% of sessions (8% double-rated) for 5 counselors; and counselors and teens provided ratings on each of 492 sessions. GP-GL taps: reinforcement for deviancy, reinforcement for positive behaviors, rejection among members, connection to counselor, and praise provided by counselor.
Results: Across scales and raters, median α = .79 and median ICC = .62. Correlations among scales across raters were found in expected directions: **r** = -.28 - .92 (**p** < .0005). Scales for each rater were correlated with measures of quality and quantity of group interaction: **r** = -.23 - .65 (**p** < .0005). Significant mean differences between treatment groups on scales were the same for counselors and supervisors (**p** < .003). Teens rated only the deviancy scale significantly differently (**p** < .025) between groups (and were consistent with counselors and supervisors).
Conclusions: This measure offers an efficient and sound method of tracking group behaviors during substance abuse treatment so that supervisors, counselors and researchers can better understand and intervene on behaviors displayed in group settings. Monitoring such behaviors may greatly assist in reducing substance use and recidivism in these at-risk teens.
Financial Support: Supported by: R01 DA-13375 (PI-Stein)

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COCAINE BEHAVIORAL ECONOMICS: FROM THE NATURALISTIC ENVIRONMENT TO THE CONTROLLED LABORATORY SETTING.

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Aims: We previously demonstrated that behavioral economic factors predict naturalistic heroin seeking behavior that correlates with opioid seeking in the experimental laboratory. The purpose of this ongoing study is to extend those findings to cocaine abusers.
Methods: Participants who respond to advertisements for a laboratory study of cocaine self-administration first complete a behavioral economic screening interview to establish past 30-day cocaine seeking/purchasing repertoire. Questions address sources/amounts of income; price (money and time) per purchase; and frequency/amounts of cocaine purchased and consumed (confirmed with Time Line Follow Back).
Results: Among the initial 50 subjects screened, higher past 30-day illegal income and to a lesser degree, total income, are significantly ($p<.05$) correlated with more frequent cocaine purchasing (rs=.72 and .33) that, in turn, is significantly related to higher cocaine expenses (r=.44). Cocaine expenses demonstrate a significant positive association with using more cocaine daily (r=.36) and greater likelihood of a cocaine-positive urine sample (r=.31). Relative to African-Americans, Caucasian subjects report longer purchase times, Levene's $t(11.88)=-3.77$, $p<.01$. Regardless of race, higher cocaine unit prices are related to significantly longer purchase times (r=.35) and purchase amounts (r=.40). Among the first 9 completers of the laboratory study, subjects who in the naturalistic setting pay higher unit prices and have longer purchase times earn significantly more intranasal cocaine 10-mg (vs. $1 alternative) units on a choice progressive ratio schedule (rs=.79 and .78, respectively). There is also a trend for higher past 30-day total income to be associated with earning more cocaine unit doses in the laboratory (r=.66, $p<.06$).
Conclusions: In summary, increased naturalistic "investment" in cocaine (paying higher unit prices and purchasing time), enabled by higher total (especially illegal) income, predicts laboratory-based cocaine self-administration.
Financial Support: Supported by NIH R01 DA026861 and Joe Young, Sr. Funds (State of Michigan)

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EFFECT OF COCAINE ON TREATMENT OUTCOMES IN OPIOID-USING PREGNANT WOMEN.

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Aims: Cocaine use among pregnant opiate dependent patients is linked to poor outcomes during treatment. The purpose of this study, a secondary data analysis from an eight-site, double blind, randomized controlled clinical trial of methadone and buprenorphine for treatment of opioid dependent pregnant women, was to investigate whether baseline cocaine use predicted maternal treatment outcomes.
Methods: Cocaine users and non-users were compared with respect to end point drug use and change in addiction severity. General Linear Model (GLM) was used for both multivariate analysis (cocaine use prior to delivery, use of opioid before delivery and number of cigarettes smoked) and repeated measures (ASI scores).
Results: Of 175 randomized patients, 131completeded the study. Of those 55.7% (n=73) were non-users while 44.3% (n=58) had used cocaine in 30 days (baseline). Multivariate analysis showed that cocaine users were more likely to have cocaine positive urine (Cocaine User=5%, Non-user=1%, p=0.000) and positive toxicology before delivery (Cocaine user=27%, Non-user=20%). However, current cocaine users smoked fewer cigarettes in 24 hours of delivery. Compared to baseline, ASI composite scores were lower at the end of treatment for psych, drug and family in the whole group. Cocaine users had smaller changes in composite ASI psych score after treatment than non-users (p=0.001).
Conclusions: A previous report from this study showed baseline association between cocaine and measures of severity. These current results indicate that cocaine use among opioid dependent pregnant women predicts increased drug use and increased psychiatric severity supporting the need to treat these women intensively.
Financial Support: NIDA grants: RO1DA15832(SMS); RO1DA018417(GF); RO1DA015738(KC); RO1DA018410(SH); RO1DA017513(PM); RO1DA015778(MC); RO1DA015741(PS)AND RO1DA015764(HJ).

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HIGH PREVALENCE OF PARTNER VIOLENCE AMONG HIV-NEGATIVE, HETEROSEXUAL, FEMALE METHAMPHETAMINE USERS.

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Aims: The goal of this study was to determine the prevalence of partner violence in a sample of HIV-negative, heterosexual, female methamphetamine (MA) users enrolled in an HIV behavioral intervention trial in San Diego, CA.
Methods: Between 2006 and 2010, 209 HIV-negative women aged 18 and older who had recently used MA and engaged in unprotected sex completed baseline interviews on substance use, mental health, sexual behaviors, and partner violence.
Results: Of 209 women, median age was 36 years, 79.9% were unemployed, and 47.9% were never married. Ethnic composition was 36.8% white, 26.8% black, 21.1% Hispanic, and 15.3% mixed/other race. In the past 2 months, the median number of times women injected MA was 5 (interquartile range (IQR), 2-20). Over one-half (57.4%) experienced forced/coerced sex in their lifetime; 164 (78.9%) experienced physical abuse. The median number of people that perpetrated forced/coerced sex against these women was 3 (IQR, 1-5) and the median number of times this occurred was also 3 (IQR, 1-6); for physical abuse, the median was 3 (IQR, 2-5) and 10 (IQR, 4-22), respectively. Almost two-thirds (63.2%) of women reported an intimate partner (spouse, boyfriend, or regular partner) as the perpetrator of their first physical and/or sexual violent experience; 20.1% reported someone they did not know and 7.7% reported a sexual client. The prevalence of current intimate partner violence (in the past 2 months) was 19.6%. Current violence by a casual partner/stranger was reported among 8.6% of women.
Conclusions: These findings underscore the importance of providing screening for partner violence within the context of substance abuse treatment programs. Furthermore, assessing the effect of partner violence on the natural history of drug use, HIV/STI risks and other health problems in drug-using populations will facilitate the development of interventions targeting these intersecting epidemics.
Financial Support: NIMH R01MH066146, NIDA T32DA023356 & R25DA025571

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PSYCHIATRIC MEDICATION-SEEKING BELIEFS AND BEHAVIORS AMONG COLLEGE STUDENTS.

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Aims: To assess psychosocial correlates of psychiatric medication-seeking behaviors in college students, in order to identify characteristics of prescription drug misusers and subpopulations to target for prevention.
Methods: The sample included 383 participants (59.2% female) recruited from various campus locations and online classes. Participants anonymously completed self-report questionnaires, including the Medication Seeking Scale and the Medication Seeking Beliefs Scale, both created for this study, as well as the Drug Abuse Screening Test (DAST) and Michigan Alcohol Screening Test (MAST).
Results: In total, 49 students admitted misusing prescription stimulants and 15 admitted misusing benzodiazepines. There were no racial/ethnic or gender differences between misusers and non-misusers. In addition, misusers and non-misusers did not differ in their history of seeking professional help for mental health concerns. However, misusers of prescription stimulants were more likely to have health insurance ($X^2 = 3.91$, $p < .05$), and misusers of both prescription stimulants and benzodiazepines were more likely to know someone who had misused that class of medication ($X^2 = 42.37$, $p < .001$; $X^2 = 34.36$, $p < 001$, respectively). Misusers also endorsed more positive attitudes toward non-medical medication-seeking, including believing it is okay to seek medication if one does not have the relevant disorder, faking symptoms to obtain a prescription, and asking someone else to give away or sell their prescription medications (all ts significant at $p < .01$). There was a significant correlation between positive medication-seeking beliefs and reported medication-seeking behaviors for stimulants ($r = .22$, $p < .001$) and for benzodiazepines ($r = .13$, $p = .01$). The most common and most "accepted" form of medication-seeking was asking for the medication from a peer.
Conclusions: Results suggest the need for further student education regarding the dangers of psychiatric medication misuse, particularly related to seeking medication from peers.
Financial Support: University Scholars fellowship awarded to the first author by the University of Florida.

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THE INFLUENCE OF BUPROPION PRETREATMENT ON COCAINE SELF-ADMINISTRATION.

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Aims: Bupropion enhances the efficacy of abstinence reinforcement therapy for cocaine dependence. The purpose of the present experiment was to "reverse engineer" a predictive human laboratory model of combined behavioral and pharmacological therapy for cocaine dependence using these clinical findings as a reference. To this end, the reinforcing effects of intranasal cocaine were determined using concurrent progressive-ratio schedules in which subjects chose between doses of cocaine (4 [placebo], 15 and 45 mg) and an alternative reinforcer ($0.25) following acute bupropion pretreatment (0, 100 and 200 mg). We hypothesized that cocaine would maintain responding to a greater degree than placebo and that bupropion would attenuate cocaine self-administration.
Methods: To date, five current cocaine-using humans completed the protocol. Up to three more subjects will be enrolled. During each session, the subjects first received a capsule containing bupropion or placebo and sampled the dose of cocaine available that day 90 minutes later. They then made six choices between that dose and money at 30-minute intervals. Data were analyzed using repeated-measures ANOVA.
Results: Initial analyses show that cocaine produced dose-related increases in break point, which were modestly, but significantly, attenuated by bupropion pretreatment at the high dose. Cocaine also produced prototypical stimulant-like subject-rated effects (e.g., ratings of Stimulated and Like Drug) which were unaffected by bupropion.
Conclusions: These data are consistent with clinical findings and demonstrate the predictive validity of a drug pretreatment/cocaine versus money choice procedure for screening putative pharmacotherapies for efficacy in combination with abstinence reinforcement in the human laboratory.
Financial Support: Supported by NIDA Grant R21 DA 024089 (WWS).

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FINAL OUTCOMES FROM AN ACCEPTANCE-BASED INTERVENTION TO IMPROVE METHADONE DETOXIFICATION SUCCESS RATES.

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Aims: Methadone maintenance (MM) is the most successful treatment available for opiate dependence, yet many MM clients wish to discontinue. Unfortunately, methadone detoxification success rates are dismal. Significant relapse rates are reported when physical withdrawal symptoms are present. Fear of the physical opiate withdrawal symptoms along with other psychological factors (e.g., anxiety, depression, irritability) are significant barriers to success. The primary aim of this study was to test the preliminary feasibility and efficacy of Acceptance and Commitment Therapy (ACT) targeting detoxification fear and avoidance of negative emotions, thoughts, or physical sensations, to improve success rates of methadone detoxification.
Methods: A stage I study to pilot test an acceptance-based opiate detoxification behavioral therapy was recently completed. Clients (N = 56) between the ages of 25 and 60 who were stable on MM via a licensed methadone clinic were randomized to receive either 24 individual therapy sessions of ACT or Drug Counseling (DC) in the context of a 6 month linear dose reduction program. Primary outcomes included opiate use as well as evaluation of theoretical processes such as experiential avoidance and detoxification fear.
Results: Evaluation of urine drug screen data across the 6 month treatment period failed to identify statistically reliable differences. However, at the end of the detoxification, the success rates, defined as opiate negative drug screen and no return to a methadone clinic, were almost double for the ACT condition (37%) relative to the Drug Counseling condition (19%). Significant treatment x time interactions were found on targeted mechanisms, Acceptance/Action ($p < .03$) and Detoxification Fear ($p < .04$), in theoretically-consistent directions.
Conclusions: ACT is a promising behavioral treatment for methadone detoxification.
Financial Support: NIDA 019436

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THE DISCRIMINATIVE STIMULUS EFFECTS OF TRAMADOL IN DRUG-EXPERIENCED HUMANS.

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Aims: Tramadol (T) is an atypical unscheduled analgesic that has evidence of both mu opioid agonist effects as well as inhibition of monoamine reuptake. Studies have shown higher acute doses exert detectable effects in drug-experienced humans, that T can attenuate opioid withdrawal, and that chronic dosing can produce opioid physical dependence. The purpose of this study was to characterize T's profile of effects with a human drug discrimination protocol.
Methods: Eight males with active opioid and stimulant use, but not dependent on either drug class, participated in this residential study. All drug administrations were double blind and oral. Subjects were trained to discriminate hydromorphone (H, 8 mg), methylphenidate (M, 60 mg), and placebo (P); each training drug was identified by a unique letter code for a subject. Testing of acquisition confirmed each participant was successful in discriminating training conditions. Discrimination testing for the following conditions then occurred: T (50, 100, 200, 400 mg), H (4, 8 mg), M (30, 60 mg), and P. Discrimination assessments were a point distribution, discrete choice, and operant responding task. Subjective and physiologic measures were also collected.
Results: Training conditions and correspondingly lower doses (M 30 mg, H 4 mg) were discriminated appropriately as their respective drug type. T 50 mg was identified as placebo like on discrimination assessments. Higher doses of T (200, 400 mg) were identified as opioid (H) like more than P like; only the T 400 mg dose was discriminated as stimulant (M) like (and this was at a low rate). Subjective reports tended to follow the same pattern as seen for discrimination tasks.
Conclusions: These findings extend previous work with T, and show that humans discriminate acute doses of T as opioid-like. While T exerts monoamine reuptake blockade, it is not discriminated as M-like. Results provide further evidence that higher acute doses of T have an opioid profile of effects, suggesting it may have abuse liability in certain populations.
Financial Support: NIDA grants DA018125, DA023186

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WEIGHT CONTROL, DEPRESSION AND GAMBLING ASSOCIATED WITH RISK OF NONMEDICAL PRESCRIPTION STIMULANT USE AMONG PRE-TEEN AND TEEN GIRLS.

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Aims: The increasing nonmedical use of prescription stimulants among youth is considered a public health threat by many, with girls misusing at a higher rate than boys (CASA, 2003). We consider the associations between weight control behaviors, depression, gambling, and nonmedical use of prescription stimulants among girls.
Methods: The National Monitoring of Adolescent Prescription Stimulants Study (N-MAPSS) assessed the medical and nonmedical use of prescription stimulants among youth 10 to 18 years of age via an entertainment venue intercept method in 10 US metropolitan areas (N=5,423; 2,753 female). We tested a model of lifetime nonmedical use of prescription stimulants among the 437 girls who said that they had ever used a prescription stimulant. Age (mean 15.6), taking prescription stimulants to promote weight control(22%), number of weight control behaviors (mean 1.22, range 0 - 5), one or more depressive symptom in any two week period in the last year (74%), and internet gambling(5%)were included in the model.
Results: The final model fit the data very well (AUC=0.791; -2 Log Likelihood 474.67). With every increased year of age, the risk of lifetime nonmedical use increased 29%(OR 1.292, 95% CI 1.14, 1.47). With every additional weight control behavior, the odds of nonmedical use increased 39% (OR 1.386, 95% CI 1.13, 1.71). Endorsing a depressive symptom increased the odds of lifetime nonmedical use of prescription stimulants almost 3 times (OR 2.74, 95% CI 1.61, 4.67). Taking prescription stimulants to control weight increased the odds of lifetime nonmedical use 3.4 times (OR 3.41, 95% CI 1.69, 6.89). Risk of lifetime nonmedical use for the 22 girls who endorsed internet gambling was increased by almost 5 times (OR 4.91, 95% CI 1.51, 16.02).
Conclusions: Experiencing depressive symptoms, taking efforts to control weight, internet gambling and growing older all increase the risk of nonmedical use of prescription stimulants among girls.
Financial Support: Contract through Pinney Associates with funding from Shire Pharmaceuticals.

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KNOCKDOWN OF SEROTONIN (5-HT) 5-HT2C RECEPTOR IN THE NUCLEUS ACCUMBENS DECREASES COMPULSIVE COCAINE-SEEKING BEHAVIOR.

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Aims: Alterations in the balance of functional activity within the 5-HT system are hypothesized to underlie impulse control and vulnerability to addictive disorders. The 5-HT2CR regulates many behavioral and neurochemical effects of cocaine as well as impulsivity, yet how the 5-HT2CR modulates the relationship between impulsivity and cocaine addiction is not well understood. The purpose of this study was to assess the role of the 5-HT2CR in the nucleus accumbens shell (NAcSh) in the sensitivity to cocaine-taking and –seeking in relation to the expression of impulsivity traits.
Methods: Recombinant AAV vectors were constructed with a separate expression cassette for eGFP and shRNA directed at the 3' untranslated region of the rat 5-HT2CR to decrease expression of all endogenous 5-HT2CR isoforms. The 5-HT2CR shRNA-AAV-eGFP viral vector was bilaterally infused into the NAcSh of male rats, while control animals received bilateral intra-NAcSh infusions of AAV-eGFP. Rats were trained in the 1-choice serial reaction time task. Rats were then trained to self-administer (SA) cocaine (0.25 mg/kg/inf; 180 min/day; FR1-5). Once stable cocaine SA on an FR 5 schedule was achieved, extinction burst responding was tested 24 hrs after a cocaine (0.25 mg/kg/inf) SA session.
Results: Premature and perseverative responses were elevated and suppressed, respectively, in NAcSh 5-HT2CR knockdown rats indicating enhanced impulsivity and diminished compulsivity, respectively. Knockdown of NAcSh 5-HT2CR did not alter acquisition rate of cocaine SA. Extinction burst responding and reinforcement threshold was, however, lower in rats with NAcSh 5-HT2CR knockdown versus control rats.
Conclusions: 5-HT2CR in the NAcSh exerts oppositional control over impulsivity and compulsivity and is critical to the development of compulsive cocaine-seeking behavior.
Financial Support: Jeane B. Kempner Scholarship, DA06511, DA024157, DA020087, DA000403

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NEUROPEPTIDE Y DECREASES THE EXPRESSION OF COCAINE-INDUCED CONDITIONED PLACE PREFERENCE IN RATS.

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Aims: Neuropeptide Y (NPY) is a neurotransmitter that acts on the neural substrate that underlies drug use and dependence. We tested the hypothesis that ICV NPY administration attenuates the expression of cocaine-induced conditioned place preference (CPP) in rats with a 3-wk history of cocaine exposure.
Methods: Male Long-Evans rats were exposed to daily injections of cocaine (COC), or vehicle (VEH), for 21 days using an escalating cocaine dose regimen (5 to 30 mg/kg, IP). CPP training occurred over the last 4 days of drug treatment and involved 2 conditioning sessions a day: one session with COC or VEH and one session with saline. We used a two-chambered CPP apparatus in which each chamber had a different visual context. Rats were assigned to receive daily COC or VEH in the 'drug-side' of the apparatus. Half of COC-treated rats received all of daily COC injections in the 'drug-side' (COC-PAIRED), while the other half, a preference control group, received daily COC in either the 'drug-' or 'non-drug-side' (COC-RANDOM). VEH-treated rats, a cocaine-history control group, received VEH on the 'drug-side' (VEH-PAIRED) on all 4 days. CPP testing was conducted 1, 7, and 21 days after the last drug treatment. ICV NPY (0, 0.1, 0.3 or 1 nmol in 5µl) was administered 30 min before the 1-day CPP test.
Results: NPY decreased the expression of CPP in COC-PAIRED rats in the 1-day test; rats receiving 0.1 and 0.3 nmol NPY showed less CPP compared to rats receiving 0 and 1.0 nmol NPY. NPY produced no effect on CPP in rats in the COC-RANDOM and VEH-PAIRED groups and these rats showed no preference for either side on any test day. It is interesting that rats in the 0.1 and 0.3 nmol NPY COC-PAIRED groups failed to show CPP at later tests, although rats in the 0 and 1.0 nmol NPY COC-PAIRED groups continued to show CPP at later tests.
Conclusions: These results support the idea that central administration of NPY decreases the strength of cocaine-associated cues to induce cocaine-driven behavior.
Financial Support: Supported by NIH/NIDA Grant DA21261

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THE HEALTH-RELATED QUALITY OF LIFE FOR DRUG ABUSERS TEST: A VALIDATION STUDY OF THE ENGLISH VERSION IN AUSTRALIA.

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Aims: There is limited availability of specific assessment tools to evaluate quality of life of individuals who abuse drugs. The Health-Related Quality of Life for Drug Abusers Test (HRQOLDA Test) is a 20-item Likert-type instrument that has been validated in Spain to assess quality of life (QoL) in the context of dug abuse. The aim of this study is to assess whether the English version of the HRQOLDA Test presents significant validity and reliability to be used as an assessment tool in English speaking populations.
Methods: 120 participants who satisfied criteria for substance-related disorders (DSM-IV) were interviewed in outpatient and inpatient facilities in the Sydney West Area Health Service, Australia. Participants completed the English versions of the HRQOLDA Test and the World Health Organization QoL questionnaire (WHOQOL-Bref). Statistical Analyses: Reliability analyses were performed to determine Crombach's alpha. Pearson coefficients were generated to explore significant score correlations.
Results: The mean age of participants was 37.74 years, and the majority (64.17%) of participants were male. All questions of the English version of the HRQOLDA Test presented significant Crombach coefficient (0.894 and above). The overall coefficient for the 20 questions was 0.905. Significant correlations ($p < 0.001$) were detected among the HRQOLDA Test scores and the scores of all 4 areas of the WHOQOL-Bref: 0.457 (Physical); 0.51 (Psychological); 0.481 (Social Relations); 0.52 (Environment).
Conclusions: The results indicate that the English version of the HRQOLDA Test presents sound internal consistency and convergent validity properties to be used as a tool to assess QoL of individuals who abuse drugs.
Financial Support: This research study was funded by the New South Wales Health Department

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GALANTAMINE'S EFFECTS ON COGNITIVE FUNCTION IN MARIJUANA USERS.

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Aims: Chronic heavy marijuana use is associated with impairments in verbal learning and memory, sustained attention and executive functioning. Whether these deficits improve with medications targeting specific cognitive functions has not been examined in previous studies. The goal of this study was to evaluate galantamine's efficacy on selected cognitive outcomes in marijuana users. Cognitive Performance was assessed with two tests from the Cambridge Neurological Test Automated Battery: the Rapid Visual Information Processing test (RVIP), and the Stop Signal Test (SST). Galantamine is an acetylcholine esterase inhibitor that has been approved for treatment of Alzheimer's disease.
Methods: Thirty marijuana users (74% male, 82% non-white) were examined in a randomized, double-blind, parallel-group study. Participants completed an adaptation session followed by a 10-day outpatient treatment period. Participants received either 8 mg/day of galantamine or placebo. Self-report measures were collected at six time points, and cognitive assessments were given at three time points.
Results: There were no significant differences between conditions (galantamine vs. placebo) on any of the demographic or baseline variables. For self report measures, the scores for both Marijuana Craving Questionnaire [$F(5, 140) = 11.72$; $p<0.001$] and the Marijuana Withdrawal Checklist [$F(5, 135) = 6.31$; $p<0.001$] decreased over time. For the RVIP, a signal detection measure of sensitivity to the target (RVP A') increased significantly over time. Median correct reaction time also increased over time on the SST for both conditions [$F(2, 56) = 3.59$; $p < .05$]. None of these outcomes showed significant main effect for treatment or treatment-by-time interactions ($p>0.05$).
Conclusions: These findings support the safety of galantamine for marijuana users. However, no differences on cognitive performance or self-report measures were found between participants who were given galantamine and those who were given placebo.
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CHARACTERIZING BRAIN SUBSTRATES OF AFFECT DYSREGULATION IN COCAINE DEPENDENCE.

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Aims: Stress and negative affect are recognized relapse contributors in addiction. Cocaine patients may be poorly equipped to modulate responses to affective stimuli, given their documented frontal deficits necessary for regulating downstream limbic regions. Characterizing the modulatory response to negative-affect cues may help identify substance users at greater risk for relapse related to affect dysregulation. Toward this goal, we developed an affect regulation paradigm to probe the brain activity during affect regulation attempts in cocaine patients.
Methods: We used block-design BOLD fMRI to measure the brain response to aversive (injury or disease) and neutral cues while chronic cocaine users (n=5, ongoing) attempted emotional regulation. All subjects identified and used cognitive reappraisal strategies to regulate negative emotions (passive; increase; suppression). Data were analyzed within SPM5, using pre-planned contrast analyses between conditions.
Results: Passive>Neutral contrast significantly activated left amygdala ($P_{corrected}<0.001$; $t=9.59$), whereas Suppress>Passive contrast revealed activation in mPFC ($P_{corrected}=0.007$, $t=4.17$) and attenuated amygdala ($P_{corrected}=0.002$; $t=-3.52$). Suppress>Increase contrast yielded pronounced activation in dmPFC ($P_{corrected}=0.002$; $t=6.11$) in cocaine patients (all k=>20 contiguous voxels).
Conclusions: Modulatory attempts during exposure to aversive stimuli recruited mPFC, an influential region in top-down modulatory system. Further, the paradigm revealed attenuated amygdala activation, suggesting the paradigm's capacity to measure brain activation associated with affect regulation in cocaine patients. These neuroanatomical circuits involved in affect regulation may be used as a marker of relapse vulnerability and a potential treatment target.
Financial Support: NIDA (R01DA10241, R33DA026114, R21DA025882, P60DA005186, P50DA012756); VAMC VISN4 MIRECC

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ADDRESSING INTIMATE PARTNER VIOLENCE PERPETRATION IN SUBSTANCE USE DISORDER TREATMENT PROGRAMS IN CALIFORNIA.

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Aims: Substance use disorders (SUDs) and intimate partner violence perpetration (IPV-P) are co-occurring problems and research shows substance use disorder treatment programs (SUDTPs) that address IPV-P within treatment have better outcomes than programs that offer SUD treatment alone. This study examines how SUDTPs in California are currently addressing IPV-P.
Methods: We surveyed program directors of 239 substance use disorder treatment programs (SUDTPs) in the state of California (70% response rate) to examine (1) the assessment and treatment of IPV-P; (2) staff training in IPV-P; and (3) reasons why programs do not offer IPV-P services.
Results: (1) At intake, two-thirds (67%) of SUDTPs assess clients for IPV-P at least some of the time but less than half (45%) of SUDTPs assess all clients for IPV-P. Of the programs that assess for IPV-P, the majority do so using their own questions (83%), while a small percentage use a standard, published scale (16%). Nearly two-thirds (65%) of SUDTPs offer at least one batterer intervention service, including anger management. (2) The majority of SUDTPs (63%) report that staff either have no training in IPV-P, or must seek out informal training on their own. Only a small percentage of SUDTPs require all staff to have formal training in IPV-P (12%). (3) Aside from IPV-P not being the program's main focus, the most common reason given for not providing IPV-P services is a lack of staff expertise (41%).
Conclusions: The majority of SUDTPs in California are making some effort to assess for and treat IPV-P. However, less than half of programs screen all potential clients for IPV-P and only a small minority of SUDTPs have direct care staff that has received formal training on IPV-P. A lack of staff expertise on IPV-P makes it difficult for programs to offer more batterer intervention services. Efforts should be made to improve assessment and increase staff training in IPV-P.
Financial Support: Support for this study was provided by a grant from the Robert Wood Johnson Foundation.

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ALTERED BRAIN HIGH ENERGY PHOSPHATE LEVELS IN METHAMPHETAMINE-DEPENDENT WOMEN.

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Aims: Methamphetamine (MA) use is strongly associated with neurotoxic effects on human brain. While there are several published reports that MA alters brain metabolite levels assessed using proton MRS, it is unclear how MA affects brain high energy phosphate metabolism, which can be measured using phosphorus-31 (31P) MRS. This study utilized 2D phosphorus chemical shift imaging (CSI) to compare in vivo phosphocreatine (PCr) levels between healthy control (HC) and MA-dependent subjects. In addition, gender differences in MA-dependent subjects were explored.
Methods: Phosphorus spectra were acquired in 26 MA (age=33±6.5, 12 female) and 5 HC (age=34±7.5, 2 female) subjects. Imaging was completed on a Siemens 3 Tesla scanner using 2D CSI free induction decay pulse sequence with TR/TE=3000/2.3ms. Whole brain spectroscopic data were quantified using AMARES. PCr level is reported as a metabolite ratio to β-nuceloside triphosphate (β-NTP).
Results: The MA subjects showed a significant reduction in the brain PCr/β-NTP ratio compared to HC by 9.3% (p=0.02). Post-hoc analysis revealed that female MA users had significantly lower (7.5%) PCr/β-NTP ratio than male MA users (p=0.03), adjusting for the total amount of MA use.
Conclusions: These preliminary data are consistent with compromised high energy phosphate metabolism in MA dependent subjects, since PCr serves as a buffer to maintain constant adenosine triphosphate levels. The gender difference in PCr levels may be relevant to the higher rate of depression in female MA users. Lower PCr levels in female MA users might be related to the higher incidence of depression and this pattern of metabolic change has also been associated with worse outcomes in response to antidepressant treatment (Iosifescu, 2008). Further study is warranted to explore the relationship between the altered phosphorus metabolism and psychiatric symptoms.
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PRECLINICAL ANTIPSYCHOSTIMULANT AND ANTIDEPRESSANT PROPERTIES OF A MONOAMINE TRANSPORTER LIGAND IDENTIFIED VIA IN SILICO SCREENING.

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Aims: To discover and preclinically test antipsychostimulant and other CNS therapeutic lead compounds of novel molecular scaffold using computer-generated molecular models of the plasma membrane monoamine transporter (MAT) proteins.
Methods: A 3-dimensional computer model of the dopamine transporter was created and used to screen a structural library of small molecule compounds. Those predicted from the model to show high affinity were tested in vitro at the human dopamine, norepinephrine and serotonin transporters via [125I]-RTI-55 displacement and [3H]-monoamine uptake inhibition assays (one-way ANOVA, post-hoc Dunnett's). The lead compound, MI-4, was tested in the conditioned place preference (CPP), locomotion, tail suspension test (TST) and forced swim test (FST) paradigms using 6-14 mice per assay (one-way ANOVA, post-hoc Tukey's).
Results: In vitro MI-4 affinities ranged from 365 nM (hNET) to 3460 nM (hDAT). Mice receiving cocaine (10 mg/kg, i.p.) spent significantly more time in the CPP drug-paired chamber; MI-4 (10 mg/kg, i.p.) reduced cocaine's effect by half, but did not exhibit rewarding effects when administered alone. MI-4 displayed minimal effects on the locomotor activity profile (time spent grooming, ambulatory time, resting time, distance traveled). MI-4 dose-dependently reduced TST and FST immobility similar to that seen with fluvoxamine or desipramine.
Conclusions: MI-4, an ifenprodil analog, interferes with the euphoric or rewarding properties of cocaine in mice. Antidepressant properties were also apparent. MAT model virtual screening of large databases of molecules is a viable method of identifying new therapeutic lead compounds of unique scaffold.
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MEDICATION DIVERSION AMONG HIV-POSITIVE SUBSTANCE ABUSERS IN MIAMI.

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Aims: Prescription drug "diversion" — the unlawful channeling of regulated pharmaceuticals from legal sources to the illicit marketplace –- has received increased attention over the past few years. This paper focuses on a previously unstudied topic — the diversion of antiretroviral medications (ARV) for HIV –- and examines the patterns and predictors of ARV diversion among drug-involved HIV-positive individuals in Miami.
Methods: Using targeted sampling strategies, this study is enrolling indigent HIV positive substance abusers in Miami. To date, we have conducted structured face to face interviews with 222 individuals using standardized data collection instruments. Bivariate logistic regression models were developed to examine risk and protective factors for ARV diversion.
Results: The sample has a median age of 46 and 82.4% meet criteria for substance abuse/dependence. 30.6% report diverting their ARV medications in the 90 days prior to interview. Significant risk factors for ARV diversion include: homelessness, severe depression, severe traumatic stress, prescription opioid misuse and sedative misuse. Protective factors include: family support, higher HIV treatment knowledge, and more favorable attitudes toward ARVs. Among the diverters, 82.1% reported a middleman or other broker as their primary ARV buyer. Median prices obtained for 30-day supplies of ARV medications were: $150 for Atripla, $100 for Kaletra, and $80 for Combivir.
Conclusions: The health implications of ARV diversion among substance abusers are substantial. Many individuals are not consistently adhering to their medication regimens, and therefore fail to achieve the full benefits of ARV treatment. In addition, the potential for transmission of medication-resistant strains of HIV is increased. At this early stage, we have observed important differences in the street market for ARV medications, in contrast to the illicit market for abusable prescription medications. These findings will be discussed.
Financial Support: This research was supported by NIH Grant R01DA023157

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SIGMA-1 RECEPTOR FUNCTION IS CRITICAL FOR BOTH THE DISCRIMINATIVE STIMULUS AND AVERSIVE EFFECTS OF THE KAPPA-OPIOID RECEPTOR AGONIST U-50,488H.

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Aims: The present study was undertaken to identify the possible involvement of sigma receptors in the discriminative stimulus and aversive effects of U-50,488H.
Methods: Fischer 344 rats were trained to discriminate between U-50,488H (3.0 mg/kg) and saline under a fixed-ratio 10 food-reinforced schedule.
Results: The kappa-opioid receptor agonist U-50,488H produced significant place aversion as measured by the conditioned place preference procedure, and this effect was completely abolished by treatment with the putative sigma-1 receptor antagonist NE-100. In addition, phencyclidine, (+)-SKF-10,047 and (+)-pentazocine, which are sigma receptor agonists, generalized to the discriminative stimulus effects of U-50,488H in rats that had been trained to discriminate between U-50,488H (3.0 mg/kg) and saline. Furthermore, NE-100 significantly attenuated the discriminative stimulus effects of U-50,488H and the U-50,488H-like discriminative stimulus effects of phencyclidine.
Conclusions: These results indicate that kappa-opioid receptor agonists, noncompetitive NMDA receptor antagonists and sigma receptor agonists may possess similar discriminative stimulus effects in rats. Moreover, not only the discriminative stimulus effects of U-50,488H, but also the aversive effects of it may affect endogenous sigma-1 receptor systems.
Financial Support: Grants from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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VARENICLINE FOR THE TREATMENT OF METHAMPHETAMINE DEPENDENCE: A PILOT STUDY.

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Aims: In a double-blind, placebo-controlled pilot trial for methamphetamine-dependent subjects, to determine the initial efficacy of varenicline (1mg BID) for the cessation of methamphetamine use.Preclinical and clinical studies suggest that cholinergic mechanisms play a role in the neurobiology of methamphetamine dependence.Cholinergic medications may alleviate MA-associated cognitive dysfunction, thereby improving outcomes of treatment for MA dependence.Varenicline is a partial agonist at $\alpha 4\beta 2$ nicotinic receptors and a full agonist at $\alpha 7$ nicotinic receptors that has been approved for smoking cessation.
Methods: Subjects (n=20) were screened for study eligibility over a 6-visit lead in and then randomized to receive either varenicline (1mg BID) or placebo for 8 weeks in addition to weekly cognitive-behavioral therapy.Subjects visited the research clinic three times a week to provide a urine sample analyzed for methamphetamine-metabolites, complete study assessments including reports of adverse events and received once-a-week individual counseling.
Results: Compared to subjects in the placebo group, participants in the varenicline group had higher rates of retention as measured by days retained in the trial (p=0.009;21 vs 43 days) and study completion (p=0.02;10% vs 60%) with trends toward longer mean days of abstinence (p=0.09; 3.7 vs 12 days) and higher mean proportion of methamphetamine-negative urine drug screens (p=0.08;9.6% vs 31%).There were no significant differences between treatment groups with respect to changes in depression, craving, or in reported adverse events.No statistically significant main effect for varenicline in reducing methamphetamine use was observed using a generalized estimating equation.A main effect of smoking status was found in GEE indicating that smokers provided fewer MA-negative urine drug screens.
Conclusions: While the results are preliminary, this pilot trial indicates that varenicline enhances both retention and abstinence.The interplay between nicotine- and methamphetamine-dependence also suggests further investigation.
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CHILDHOOD ABUSE AND SUBSTANCE MISUSE AMONG CRIMINAL OFFENDERS.

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Aims: To test the following hypotheses among criminal offenders:
1) Childhood physical and sexual abuse (CA) will be related to symptoms of substance use disorders,
2) CA will be related to substance use consequences after controlling for substance type and frequency of use,
3) The relationship between CA and substance misuse will be greater among female offenders.
Methods: Participants were 219 male and female offenders, ages 18-58, participating in a pretrial supervision program subsequent to receiving criminal charges. The racial and ethnic composition of the sample was 28.4% White, 52.3% Black, and 19.4% other. Consenting individuals completed group-administered self-report measures. Severity of CA was derived from responses to questions from the Conflict Tactics Scale (Straus, 1979). Substance use consequences during the past six months were assessed using the Inventory of Drug Use Consequences (INDUC; Tonigan & Miller, 2002).
Results: Childhood physical abuse was associated with symptoms of alcohol use disorder. Childhood sexual abuse was associated with symptoms of drug use disorder. Both forms of CA were associated with substance use consequences after controlling for substance type and frequency of use. Gender did not moderate any of these relationships.
Conclusions: Consistent with prior findings, CA is associated with increased substance misuse among criminal offenders. The relationship between CA and substance use consequences is not mediated by substance type and frequency of use, and no relationships between CA and substance misuse among offenders are moderated by gender. Thus, CA history should be considered important to substance misuse risk among both males and female offenders.
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NEURAL REGULATION OF THE TIME COURSE FOR COCAINE CUE EXTINCTION CONSOLIDATION.

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Aims: The dorsal subiculum (dSUB) and rostral basolateral amygdala (rBLA) are neural substrates for acquisition and consolidation of cocaine cue extinction. We hypothesize that the time course of cocaine cue extinction consolidation is altered after protein synthesis inhibition.
Methods: Rats were trained to self-administer cocaine paired with cues under a second-order schedule during 1hr sessions. Next, rats received daily 1-hr extinction sessions for 3 days (no cocaine, but cues present) and patterns of extinction responding were measured in 15 min bins. Because inhibition of protein synthesis has been shown to disrupt consolidation of fear extinction, rats (n=8-9/tx) received anisomycin (ANI; 100 μg) or vehicle (VEH) bilaterally into dSUB or rBLA immediately after each extinction session to test our hypothesis.
Results: Baseline self-administration did not differ between groups. As expected, the decline in within-session extinction responses on day 1 was similar in all 4 untreated groups. Post-session ANI treatment of the dSUB, but not rBLA, on day 1 prevented the normal decline in within-session extinction responses on day 2, particularly during the first half of the 1-hr session. Responding was significantly greater during the second 15 min bin of day 2 in rats treated with ANI compared to VEH in the dSUB ($p<.01$). The normal decline in within-session extinction responses on day 3 was prevented as well by post-session ANI treatment of both the dSUB and rBLA on day 2. Notably, responding was greater in rats treated with ANI compared to VEH for the first, second and third 15 min bins for the dSUB ($p<.03$), and for the second and third 15 min bins for the rBLA ($p<.03$).
Conclusions: An analysis of the time course of changes in extinction responding suggests that the dSUB is engaged in memory consolidation following a single extinction session, whereas the rBLA is engaged only following multiple extinction sessions. Findings suggest that the dSUB and rBLA have similar but temporally distinct roles in regulating the time course of cocaine cue extinction consolidation.
Financial Support: DA 024315, SBE 0354378

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SEARCHING FOR A NEUROBIOLOGICAL BASIS FOR SELF-MEDICATION THEORY IN ADHD COMORBID WITH SUBSTANCE USE DISORDERS: AN IN VIVO STUDY OF DOPAMINE TRANSPORTERS USING 99MTC-TRODAT-1 SPECT.

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Aims: Attention-Deficit/Hyperactivity Disorder (ADHD) and Substance Use Disorders (SUD) frequently co-occur. Although several studies have shown changes in striatal dopamine transporter (DAT) density in these disorders, little is known about the neurobiological basis of the comorbidity. The aim of this study was to evaluate striatal DAT density in treatment-naive ADHD adolescents with SUD (ADHD+SUD) and without SUD (ADHD), compared to SUD adolescents without ADHD (SUD) and healthy control subjects (HC).
Methods: 62 male age matched subjects diagnosed with DSM-IV criteria were included: ADHD+SUD (n=18); SUD (n=14); HC (n=19), and ADHD (n=11). Urine tests confirmed participants' drug use. All subjects performed SPECT scans with the 99mTc-TRODAT-1 radiotracer to evaluate DAT in vivo. Biding potential (BP) was calculated to estimate DAT density/affinity in the striatum.
Results: The mean right striatum BP obtained were 1.68 (ADHD), 1.38 (ADHD+SUD), 1.19 (HC), 1.17 (SUD), and in left striatum 1.65 (ADHD), 1.39 (ADHD+SUD), 1.19 (HC) and 1.17 (SUD). The ADHD group presented significantly higher striatal DAT density compared with ADHD+SUD, SUD and HC groups. Adolescents with ADHD+SUD had significantly lower DAT density than those with ADHD, but significantly higher DAT density than those with SUD only and no significant difference from the healthy control group.
Conclusions: The ADHD+SUD group had lower striatal DAT density in comparison with ADHD patients without SUD. It is possible to speculate that the use of cannabis and cocaine is responsible for the lower striatal DAT density in this group which would help understanding the neurobiological basis for the self-medication theory in ADHD adolescents.
Financial Support: Brazilian funding sources (CAPES, FIPE/HCPA)

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RESTING STATE CONNECTIVITY BETWEEN THE AMYGDALA AND POSTERIOR CINGULATE CORTEX PREDICTS ABSTINENCE FROM CANNABIS.

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Aims: There is growing interest in studies of the brain in the resting state, which has been suggested to be useful as a biomarker of psychiatric disorders. However, little is known about the role of resting state brain function in substance use disorders (SUD). We previously reported that resting intralimbic connectivity is correlated with affective symptoms in cannabis-dependent patients. The present study investigated the association between resting amygdala connectivity and subsequent days abstinent from cannabis use. We hypothesized that increased amygdala-cortical connectivity, reflecting the potential for modulation of limbic motivational circuitry, could predict increased abstinence from cannabis.
Methods: 12 treatment-seeking cannabis-dependent patients underwent perfusion fMRI at rest prior to outpatient treatment for marijuana dependence (dronabinol or placebo). Connectivity maps of the whole brain were generated using voxelwise regression with the amygdala as the seed region. The no. of days abstinent from cannabis was calculated for 7 weeks using the Timeline Followback questionnaire. The relationship between amygdala connectivity and days abstinent was examined using linear regression in the pooled sample of 12 participants from both treatment groups.
Results: Mean no. of days abstinent was 16.08±14.96 (SD) with a range of 0-38. A positive correlation was observed between resting amygdala connectivity with the posterior cingulate cortex (PCC) and days abstinent from cannabis ($r=0.88$; $p < 0.0001$, uncorrected). (There was no statistical difference in days abstinent between dronabinol- and placebo-treated patients).
Conclusions: These results provide the first evidence that increased resting connectivity between the amygdala and the PCC may be associated with a reduced risk of relapse in cannabis dependence. These findings also suggest that studies of the resting state may hold promise in predicting outcome in patients with SUD.
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FUNCTIONAL STUDIES OF COCAINE-INDUCED INCREASES IN PREFRONTAL CORTEX MGLUR1, PI3K AND PKC EPSILON EXPRESSION FOR COCAINE-SEEKING IN MICE.

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Aims: Our previous immunoblotting studies demonstrated that the repeated non-contingent administration of cocaine (7 x 30 mg/kg) elevates prefrontal cortex (PFC) expression of Homer2, concomitant with increases in the mGluR1 subtype of Group1 metabotropic glutamate receptors (mGluRs). Group1 mGluRs are Gq-coupled receptors that activate protein kinase C (PKC) and phosphoinositide 3-kinase (PI3K) signaling through their alpha and beta-gamma subunits, respectively. The functional relevance of cocaine-induced changes in mGluR1-mediated signaling for cocaine-seeking is not known.
Methods: Immunoblotting was conducted for kinase levels in PFC tissue from C57BL/6J mice, sacrificed 3 weeks following repeated cocaine (7 X 30 mg/kg). The levels of phospho-(Ser729)PKC epsilon and phospho-(Tyr)p85alpha were also determined to index kinase activity. In the behavioral study, mice were subjected to standard cocaine place-conditioning procedures (4 X 15 mg/kg). Mice were then microinjected intra-PFC with the mGluR1 antagonist JNJ 16259685 (30 pg/side), the PI3K inhibitor wortmannin (50 ng/side) or a PKC epsilon peptide inhibitor (0.5 microliters/side) and then tested again for CPP.
Results: Withdrawal from repeated cocaine significantly elevated and reduced respectively PFC indices of PI3K and PKC epsilon activity. While PKC epsilon blockade did not affect the cocaine CPP, the magnitude of CPP was potentiated by mGluR1 blockade. In contrast, PI3K blockade elicited a conditioned place-aversion.
Conclusions: Long-term withdrawal from repeated cocaine shifts mGluR1-mediated signaling through the beta-gamma subunit of Gq. While mimicking the cocaine-induced decrease in PFC PKC epsilon activity is insufficient to alter cocaine-seeking, preventing the rise in PFC PI3K activity produces a cocaine-aversive state. If relevant to humans, these data implicate drug-induced increases in mGluR1/Homer2 signaling through PI3K within the PFC as an important neural substrate mediating cocaine-seeking behavior in addiction.
Financial Support: NIDA grant DA024038 to KKS and NRSA to AWA.

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THE DARK SIDE OF SNIFFING: PAINT COLOR AFFECTS INTOXICATION EXPERIENCES AMONG ADOLESCENT INHALANT USERS.

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Aims: Inhalant abuse among adolescents is a significant health concern in many countries, however limited research has explored whether the intoxication experience differs between commonly used inhalants. The aim of the present study was to examine how exposure to different types of paints (chrome vs. non-chrome) were experienced by adolescent users.
Methods: 16 adolescent (aged 15-19 years) regular inhalant users completed a semi-structured questionnaire inquiring about their inhalant use. Participants were divided into two groups based on paint colour preference (chrome paints [n = 10] and non-chrome paints [n = 6]), and were compared using appropriate statistical tests.
Results: Relative to non-chrome users, the chrome-using group were more likely to report deliberately inhaling to experience altered perceptions (such as visual and auditory hallucinations). In addition, a significantly greater proportion of chrome users reported that the perceptual alterations they experienced after sniffing paint differed between paint colours, with chrome colours being associated with more vivid hallucinations.
Conclusions: While both chrome and non-chrome users reported a comparable level of pleasure from paint sniffing, chrome paint users were more likely to be motivated by the potential to hallucinate. Our findings suggest that the type of inhalant used is an important consideration that may have relevance to clinical treatment.
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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INCREASE OF BRAIN ACTIVITY AND CHANGE IN REM SLEEP INDUCED BY KETAMINE: POSSIBLE RELATIONSHIP TO ITS PSYCHOTOMIMETIC EFFECT.

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Aims: Ketamine, is an intravenous anesthetic that shows psychotomimetic effects in human. This study was designed to assess the effects of ketamine on the discriminative stimulns effect, sleep behavior, and brain activity.
Methods: The discriminative stimulus effects of ketamine were investigated by rats trained with ketamine (5 mg/kg i.p.) under a fixed-ratio 10 food-reinforced schedule. The receptor binding-displacement assay was performed by incubating the whole brain sample of naive mice together with ketamine. The sleeping behavior and the brain activity were determined by using the electroencephalography/electromyography (EEG/EMG) and functional magnetic resonance imaging (fMRI), respectively. The level of protein kinease C was measured by using Western blot analysis.
Results: We demonstrated that both PCP and MK-801, the NMDA receptor antagonists, substituted for a ketamine cue. The receptor binding assay showed that ketamine displaced the [3H] MK-801 binding. Furthermore, the higher doses of ketamine bind to μ- and κ-opioid receptors. We found that ketamine increased REM, but not non-REM sleep stage. Additionally, fMRI analysis showed that ketamine enhanced the brain activity in the cingulate cortex (CG) and amygdala. Interestingly, ketamine produced a significant increase in the level of p-PKCγ in the brain.
Conclusions: We demonstrated that ketamine showed the affinity for not only NMDA receptors but also opioid receptors. Moreover, ketamine changed the sleeping behavior and brain activity with enhanced PKCγ activity in the brain. Furthermore, ketamine-induced discriminative stimulus effects are likely to reflect the PCP-like psychotomimetic effects.These findings may explain the mechanisms of ketamine-induced psychotomimetic effects.
Financial Support: This research was supported by grants from The Ministry of Education, culture, Sports, Science and Technology of Japan.

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NICOTINE EFFECTS ON DEFAULT MODE AND EXTRA-STRIATE RESTING STATE NETWORKS.

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Aims: The positive cognitive effects of nicotine on attention may contribute to the initiation and maintenance of smoking. Studies have shown that nicotinic agonists decrease activity in parietal and increase activity in extra-striate cortex while subjects perform tasks involving attention. The overlap between parietal lobe deactivations and the "default mode network (DMN)" suggests that nicotine may enhance cognition by shifting attention away from internal processes generated by DMN toward external processes. At the same time, nicotine may facilitate visual attention by increasing activity in extra-striate visual cortex. The DMN and extra-striate systems are among several resting state networks that are robust and observed consistently across subjects. It is unknown, however, if nicotine directly affects DMN and extra-striate resting state activity in the absence of effortful processing.
Hypotheses: Nicotine suppresses activity in DMN and enhances activity in extra striate resting state cortex in the absence of an external visual task.
Methods: Within-subject, single-blinded, counterbalanced study of nineteen non-smoking subjects who underwent resting functional MRI scans before and after 7 mg nicotine or placebo patch. Group independent component analysis was performed. The DMN component was identified by spatial correlation with a reference DMN mask. A visual attention component was identified by spatial correlation with an extra striate mask. Analyses were conducted using Statistical Parametric Mapping 8.
Results: Nicotine was associated with decreased activity in regions within the DMN and increased activity in extra striate regions.
Conclusions: Suppression of DMN and enhancement of extra striate resting state activity in the absence of visual stimuli or effortful processing suggests that nicotine's cognitive effect involves a shift from networks that process internal to those that process external information. This is a potentially significant neural mechanism contributing to the initiation and persistence of nicotine addiction.
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DIFFERENCES IN PARENTING IN SMOKERS VS. NON-SMOKERS DURING PREGNANCY.

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Aims: Mothers who use substances during pregnancy face numerous challenges that may thwart their ability to parent effectively. The examination of prenatal smoking on parenting outcomes may inform the development of more targeted intervention for parent-child dyads of mothers who smoked prenatally. While multiple studies have investigated ilicit drug use during pregnancy and parenting, licit, and more common drugs such as nicotine have not been as well studied to date.
Methods: Maternal reported parenting practices such as disciplinary techniques were examined in moms that smoked vs. did not smoke cigarettes while pregnant in a sample of n=306 children enrolled in an ongoing longitudinal investigation of preschoolers.
Results: Moms that did not smoke during pregnancy were significantly less likely than moms that smoked to give (mean frequency):
verbal dispraises (p<.001);
spank (with hand) (p=.016);
deny privileges (p=.003);
leave a child in a car without an adult (p=.006);
or ever leave bruises (OR 6.35, 95% CI 2.20-18.29, P=.001).
Quantity smoked (<10 or >10 cigarettes/day) was associated with significantly greater frequency of spanking, denial of privileges, and verbal rejection.
Conclusions: While further studies are warranted to investigate the sources of the differences in parenting found, the current study findings suggest that mothers that smoked utilize harsher and more punitive parenting that those who did not, with dose-dependent effects. Study results may inform targets for early dyadic psychotherapy/psychosocial interventions.
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and R01 MH 64769, Joan Luby, M.D.

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NEURAL CORRELATES OF REWARD PROCESSING IN METHAMPHETAMINE USE.

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Aims: Methamphetamine use is associated with alterations in multiple brain circuits. The Monetary Incentive Delay (MID) task, together with fMRI has been used to elucidate the neural circuitry of reward processing in healthy and psychiatric populations. We aimed to define the neural correlates of the stages of the reward response under different motivational conditions in chronic methamphetamine use with the MID Task and fMRI.
Methods: 12 methamphetamine dependent (MA) and 12 healthy (HC) males were administered the MID task during fMRI scanning. The MID task allows for the dissociation of neural activity during the anticipation and consumption reward under positive and negative monetary contingencies. Neural activity during the performance of this task was compared between groups.
Results: HC and MA participants exhibited significant differences in neural activity while performning the MID task. During anticipation of potential monetary gain, HC participants showed increased activation of ACC and NAcc, two reward-related brain regions, whereas MA participants exhibited decreased activation in temporal and parietal regions. During anticipation of potential monetary loss, HC, but not MA, participants showed engagement of insula and prefrontal cortex. Similar to the anticipatory period, the consummatory period of monetary reward processing was characterized by significant group differences in neural activity.
Conclusions: Our use of a well-defined fMRI task of reward processing allowed for the investigation of the alterations in the neural circuitry for reward in chronic methamphetamine use. We demonstrated MA participants failed to activate the normal neural circuitry for reward and instead engaged of alternate brain regions. Therefore, methamphetamine use is associated marked alterations in the neural processing of monetary rewards.
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WHICH PSYCHO-SOCIAL CHANGES AFFECT DRUG USE AMONG PROBATIONERS?

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Aims: Studies have found that drug users improve in their overall psycho-social functioning during the course of treatment (Arnold, 2007; Raynor, 2007). Prior research has examined these changes in the domains of substance use, anti-social cognition, anti-social associates, family and marital relations, employment, and leisure and recreational activities. Few studies have assessed which aspect of psycho-social functioning has the greatest impact on changes, but little is known about which factors are most important in reducing substance abuse.
Methods: The study uses four waves of data from a randomized controlled trial (baseline, 3-, 6-, and 12-months post randomization) to examine the impact of various psychosocial needs among a sample of 250 drug-involved probationers. These data were obtained from the Criminal Thinking Scale, Orientation of Social Support, Community Assessment Inventory, and life history event calendars. A series of negative bi-nominal regression models were conducted to examine changes in different need factors (anti-social cognition, anti-social associates, family and marital relations, employment, alcohol use, and leisure and recreational activities), on the number of self-reported days of substance use, while controlling for other individual-level variables.
Results: Multivariate analyses found that probationers who experienced a decrease in antisocial associates over time had the greatest reduction in self-reported drug use ($p<.001$), followed by those who enhanced their work performance ($p<.001$) and decreased their alcohol use ($p<.001$). Other factors such as antisocial cognition, family and marital, and leisure and recreation were unrelated to frequency of self-reported drug use.
Conclusions: These findings suggest that certain dynamic need changes are responsible for greater reductions in drug use than others, and that interventions should emphasize improved functioning in reduced antisocial peers, improved employment prospects, and decreased alcohol use.
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TEMPORAL CHANGES IN INITIATION OF INJECTION USE IN HEROIN USERS IN MALAYSIA, 1968 TO 2010.

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Aims: To explore factors associated with the transition from smoked to injection heroin use (IDU) and temporal changes over the past 40 years in the transition.
Methods: Timelines drug use histories detailing age of first use of heroin and of misuse of other substances (cigarettes, marijuana, alcohol, benzodiazepines, amphetamine-type stimulants, buprenorphine), age of initiation of IDU and reasons for initiating IDU were recorded by a single psychiatrist from 423 patients (all male) enrolling in 3 clinical trials in Muar, Malaysia between 2003 and 2010. We evaluated the cumulative proportions of study participants initiating each substance and initiating IDU since 1968 and compared mean years from first heroin use to initiation of heroin IDU for four subcohorts of patients based on their year of IDU initiation (1969-1988; 1989-1995; 1996-1999; and 2000-2009).
Results: 420/423 (99%) of the sample initiated heroin use via chasing or smoking; 282/423 (67%) initiated IDU by 2009. Heroin use and IDU accrued steadily and uniformly between 1968 and 2009, with a lag for IDU. Mean (SD) years from initiation of heroin use to initiation of IDU was 6 (4) from 1968 to 1988, 7 (6) from 1989 to 1995, 7 (6) from 1996 to 1999; and 9 (8) from 2000 to 2009. Most common reasons for initiating IDU included developed tolerance to heroin (111/214, 42%), heroin shortage (62/214, 24%), heroin cost (37/214, 14%), and peer influence (37/214, 12%).
Conclusions: Although almost all patients first used heroin by smoking, 67% switched to IDU on average 7 years after their first heroin use. The continued steady increase in the numbers of heroin users transitioning to IDU between 1988 and 2009—despite the onset of the AIDS epidemic in Malaysia (the first AIDS case was reported in Malaysia in 1988; by 1994, HIV seroprevalence was 40% among IDUs in rehabilitation centers, and IDU accounted for >75% of HIV cases)—is particularly troubling and points to the importance of improving education, outreach, counseling, drug treatment and other harm reduction efforts in Malaysia.
Financial Support: NIDA 1R01DA14718, 2R01DA014718, K24DA000445

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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 propofol, decontrol of 6-beta-naltrexol and amendment to CFR so as to allow generic products of dronabinol in sesame oil into schedule III is currently ongoing.
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) 2,5-Dimethoxy-4-chlorophenethylamine (2C-C), 2,5-Dimethoxy-4-methylphenethylamine (2C-D), and 2,5-Dimethoxy-4-ethylphenethylamine (2C-E), 2,5-dimethoxy-4-iodoamphetamine (DOI), 2,5-Dimethoxy-4-chloroamphetamine (DOC) for possible control under the CSA. Upon completion, these data will be sent to the Department of Health and Human Services for scientific and medical evaluations and scheduling recommendations for control under the CSA.
Conclusions: 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.
Financial Support: Drug Enforcement Administration

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CONTRACEPTIVE ADHERENCE AND METHOD CHOICE AMONG WOMEN WITH DRUG AND ALCOHOL PROBLEMS: A SYSTEMATIC REVIEW.

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Aims: We undertook a systematic review in order to answer the following 2 questions: 1) Are women with drug and alcohol problems less adherent with contraception, and 2) What are the most common methods among women with drug and alcohol problems?
Methods: MEDLINE was searched using the following keyword and MeSH heading search strategy: "Contraception AND Substance abuse disorder". To be included in the systematic review, articles had include participants with drug and alcohol problems and contraceptive choices had to be measured.
Results: A total of 96 articles were retrieved of which 8 met our inclusion criteria. 4 articles had comparison groups. Overall women with drug and alcohol problems were less adherent with contraception with adherence rates ranging from 26 to 73%. Non-adherence appeared to vary by method. Compared with other methods, condom use was higher among women with drug and alcohol problems whereas rates of long acting contraceptive use were very low.
Conclusions: Women with drug and alcohol problems are less adherent with contraception and therefore at higher risk of unintended pregnancy.
Financial Support: None

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TURNING POINTS IN DRUG USE TRAJECTORIES: PROPOSITION 36 PARTICIPANTS' PERSPECTIVES.

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Aims: Rooted in the life course theory, "turning points" has been used to explain and characterize major changes in drug use trajectories. However, the same life event may trigger a turning point for some individuals, but not others. This study explores the developmental processes and underlying mechanisms involved in turning points, particularly for participants in California's Proposition 36 program (Substance Abuse and Crime Prevention Act or Prop 36; offers adults convicted of non-violent drug-related offenses drug treatment in the community in lieu of incarceration).
Methods: Two-hour in-person interviews, including semi-structured and structured (e.g., Addiction Severity Index, Natural History Interview) components, were conducted with 34 Prop 36 participants approximately 5 years after their index treatment. Interviews explored turning points in participants' drug use, factors contributing to these changes, and individuals' experiences in Prop 36. Interviews were audio-recorded, transcribed, and analyzed using ATLAS.ti.
Results: The sample was comprised of males (74%) and females (26%); average age was 42 years (26-64 years); primary drug at intake included methamphetamine (67%), marijuana (15%), cocaine (12%), and heroin (6%); and participants were White (47%), Hispanic (41%), Black (9%), and Native American (3%). Preliminary emerging themes include factors contributing to turning points in drug use (e.g., conscious decision to change, avoidance/fear of incarceration, a loved one, being "tired" of the lifestyle), factors influencing and sustaining behavior changes (e.g., structure, family support, avoidance of drug-using friends, keeping busy to refrain from using, participation in self-help), and the processes facilitating turning points (e.g., reflecting on one's life, "humbling" oneself).
Conclusions: Ultimately, findings from this study may help to inform clinical intervention strategies, policies and further research on recovery from substance abuse.
Financial Support: This study was supported by NIH/NIDA R03DA025291, P30DA016383 and K05DA017648.

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IMPACT OF COCAINE USE ON METHADONE AND BUPRENORPHINE CONCENTRATIONS IN HIV-INFECTED AND UNINFECTED PATIENTS.

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Aims: Cocaine use during opioid agonist treatment (OAT) with methadone or buprenorphine (bup)/naloxone decreases methadone and bup concentrations in human laboratory settings and may lead to poor treatment outcomes. We sought to determine the impact of cocaine use on methadone and bup concentrations in HIV-infected and uninfected patients in clinical care.
Methods: Patients were enrolled if they were on OAT for over two weeks with self-report and urine toxicology (Utox)-confirmed cocaine use. R- and S-methadone or bup and norbuprenorphine (norbup) concentrations were assessed at 0.5, 1, 2, and 24 hours after OAT dosing by mass spectrometric methods. The same protocol was repeated after self-reported and Utox-confirmed cocaine abstinence. Each patient served as their own control. Methadone and bup concentrations were standardized to respective doses of 80mg and 16mg. Crude and multivariate analyses comparing methadone and bup concentrations for cocaine use vs. abstinence were run, stratified by HIV status, using paired t-tests and ANOVA.
Results: 33 patients completed the study; 16 on methadone (6 HIV-infected) and 17 on bup/nx (8 HIV-infected); 35% female, 48% Caucasian, mean age 45 yrs. 86% (12/14) of HIV-infected patients were on antiretrovirals (ARVs). In the presence of cocaine, compared to cocaine abstinence, peak R-methadone (244 vs 297 ng/mL, p=0.03) and peak S-methadone (285 vs 339 ng/mL, p=0.03) concentrations were reduced in HIV-uninfected patients but not in HIV-infected patients. Peak bup and norbup concentrations were unchanged regardless of HIV status.
Conclusions: Cocaine use may decrease methadone concentrations in HIV-uninfected patients and does not effect bup concentrations; yet, results may be limited by small sample size. Further research is needed to confirm these findings and to determine if HIV infection or ARVs play a role in attenuating cocaine's effect on methadone levels.
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PARENTAL MONITORING AND DELAY DISCOUNTING: ASSOCIATED RISK FACTORS FOR ADOLESCENT CIGARETTE SMOKING.

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Aims: Parental influence and social peer networks are two of the most consistent predictors of cigarette smoking during adolescence(Flay et al., 1994). For example, having parents who smoke and having peer friends who smoke are both highly predictive of cigarette smoking initiation during adolescence. Additionally, parental monitoring (i.e., the degree to which parents monitor the activities of their children) provides protective effects against initiation of smoking (e.g., Piko & Kovacs, 2009). For the current study we examined the relationship between a behavioral characteristic of mothers (i.e., the degree to which they discounted by delay—an index of impulsive decision-making) as related to their children's ratings of parental monitoring. It was hypothesized that greater discounting would be associated with less monitoring. Additionally, to further explore risk of smoking, we obtained child self-reports about the proportion of their friends who smoked.
Methods: The study participants were 55 mother/child dyads, with children between 13 and 15 years of age. All participants completed a single laboratory session of approximately 2 hrs.
Results: Regression analyses revealed that, as hypothesized, delay discounting by mothers was a significant predictor of parental monitoring ($F = 5.94$, $p = .018$). Moreover, children who reported less monitoring reported that a greater proportion of their friends smoked ($F = 7.97$, $p = .007$), further demonstrating an increased risk of smoking.
Conclusions: These findings suggest that delay discounting may be a behavioral characteristic that influences parental monitoring. Future research and efforts to improve monitoring may benefit from a better understanding of how delay discounting by the parents contributes to this important parenting variable.
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COCAINE, METHAMPHETAMINE, ALCOHOL AND MARIJUANA ENHANCES HIV INFECTION AND DISEASE PROGRESSION: ROLE OF NEUROTOXIN ARACHIDONIC ACID.

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Aims: Aims: HIV infection and disease progression is enhanced by substance abuse, which leads to immune dysfunction. Neurotoxins such as arachidonic acid are secreted in plasma due to substance abuse (cocaine, METH, alcohol and marijuana) which may predispose to viral replication and disease progression. In this study, our aim is to examine the exacerbating effect of neurotoxin, arachidonic acid and its interactive role in plasma among HIV positive and negative substance abusers.
Methods: Methods: Plasma samples were collected from normal, HIV positive, substance abusers (cocaine, METH, alcohol and marijuana), and desired combinations of HIV positive and cocaine, METH, alcohol, marijuana abusers. Samples were analyzed by western blotting to determine cyclooxygense -2 (COX-2) and prostaglandin E2 (PGE2) protein expression. The level of PGE2 production and arachidonic acid concentration was evaluated by ELISA
Results: Results: Our results indicate that HIV infected with cocaine, METH, alcohol and marijuana abusers significantly upregulated COX-2 and PGE2 protein expression, as well as the level of arachidonic acid concentration compared to HIV infected nondrug using or HIV negative drug using populations.
Conclusions: Conclusions: Taken together, our results suggest that HIV infected with substance abuse populations have increased plasma arachidonic acid and byproducts COX-2 and PGE2, which affect immune function. The clinical implications of these findings warrant further study.
Financial Support: Financial Support: Supported by NIH grants DA012366, DA 021537, DA 025576 and R01MH08529

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ANALYSIS OF HERBAL "SPICE" MIXTURES CONTAINING SYNTHETIC CANNABINOIDS USING SOLID-PHASE MICRO-EXTRACTION AND GAS CHROMATOGRAPHY/MASS SPECTROMETRY.

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Aims: Smokable herbal mixtures containing non-controlled synthetic cannabinoids have been sold on the Internet and in various retail shops, and their prevalence and abuse has increased dramatically. In response to the perceived risk associated with these products the US Drug Enforcement Administration used its emergency scheduling authority to temporarily control five synthetic cannabinoid used in their manufacture. However, there are hundreds of cannabimimetic compounds, in several chemical classes, and it might be anticipated that new substances will appear in similar formulations. This presents a challenge for the forensic and toxicological identification of new substances for the prompt assessment of risk and, where necessary, implementation of control measures law enforcement agencies. To address the need for rapid analysis of herbal formulations sold as incense, but suspected to contain synthetic cannabinoids, an automated solid-phase microextraction and gas chromatography/mass spectrometry (SPME-GC/MS) method was developed.
Methods: Briefly, the method involved heating herbal samples to 200 °C, sampling the head space with a carboxen/polydimethylsiloxane SPME fiber, desorbing the fiber onto a DB-5MS capillary column, and eluting the analytes using a temperature gradient from 40 to 300 °C while the MS scanned from 50 to 500 m/z.
Results: The analytical approach allows for the detection of JWH-018 and other synthetic cannabinoid analogs, from small quantities of materials (~50 mg), without requiring extraction, concentration or derivatization. Analysis of over 20 products, obtained from retail stores in North Carolina, revealed the presence of at least one synthetic cannabinoid in each product. Several products had two or more analogs, and one product appeared to have a novel, previously unreported JWH analog present.
Conclusions: The SPME-GC/MS approach allows for rapid analysis, detection, and mass spectral confirmation of synthetic cannabinoids in herbal formulations.
Financial Support: Supported by NIDA-N01DA-0-7301.

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NEGATIVE REINFORCEMENT LEARNING IS IMPAIRED IN ADULTS WITH SUBSTANCE DEPENDENCE.

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Aims: Substance dependent individuals (SDI) often do not make good long-term decisions on the Iowa Gambling Task (IGT). The aim of this study was to explore whether poor decision making might be related to deficits in learning. Positive reinforcement is salient in early stages of addiction, while negative reinforcement may be important in persistence and relapse. Little research has examined negative reinforcement learning in SDI. We compared positive and negative reinforcement learning on a modified IGT in SDI compared to controls, and explored whether groups differed in learning from decks varying only on frequency compared to magnitude of gains and losses over time.
Methods: 31 patients in treatment for SD were compared with 28 community controls screened for drug dependence on a modified IGT that offered cards from each of four decks, one at a time, for the subject to press a button to choose to PLAY or PASS. This modification standardized the order in which subjects explored the decks and required an active response for each card. We compared the groups over time in learning to PLAY cards from good decks and to PASS cards from bad decks.
Results: SDIs and controls did not differ in PLAY responses to good decks, but differed significantly in learning to PASS on bad decks. Further analysis on PASS responses to bad decks revealed group differences related to magnitude information ($p < .01$), but not to frequency information. Group differences were also found on Delayed Discounting ($p < .01$) and self-reported impulsivity (Barratt Impulsivity Scale; $p < .001$), but performance on the modified IGT did not correlate with either in the SDI group.
Conclusions: SDIs were impaired in learning to pass cards on the deck that was disadvantageous because of the magnitude of loss. This deficit in negative reinforcement learning is a potential mechanism for poor decision-making on the IGT and may contribute to persistence of addiction and relapse among SDIs.
Financial Support: This work was supported by NIDA grants DA024104 and DA027748 to Dr. Tanabe.

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HIGH RISK HIV BEHAVIORS IN PRESCRIPTION OPIOID, IV HEROIN, AND NON-IV HEROIN USERS.

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Aims: Extensive evidence confirms a strong link between illicit opioid use and infectious diseases. Little research has addressed whether rates of HIV risk behaviors reported in heroin users is similar for prescription opioid (PO) users. The aim of the current analyses is to compare high risk HIV behaviors by main opioid of abuse and by injection drug use.
Methods: Baseline and post-treatment data were collected in a current NIDA-sponsored study of 16-weeks of combined pharmacotherapy and behavioral interventions for the treatment of opioid dependence. Opioid-dependent individuals were distinguished by self-reported primary problem opioid and by injection use to create three opioid use groups, PO ($n = 50$), IV Heroin ($n = 33$), and Non-IV Heroin ($n = 31$).
Results: Significant group differences were found at baseline for injection use for the last 6 months ($p < 0.00$) and for the last 30 days ($p = 0.02$), and at post-treatment for the last 6 months ($p < 0.00$). Comparisons of high risk sexual behaviors document significant group differences at baseline in unprotected sex with IV drug users in the last 6 months ($p = 0.01$). Other comparisons, including changes in baseline to post-treatment risk behaviors, will be presented.
Conclusions: These findings support previous research showing increased HIV risk behaviors associated with injection drug use. No differences by type of opioid used were found, suggesting that the recent increase in PO use will require similar high risk HIV behavior education during treatment as that provided for heroin users.
Financial Support: NIDA R01 DA 020210

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LONGITUDINAL HIV RISK IN YOUTH REFERRED TO SUBSTANCE TREATMENT.

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Aims: To compare longitudinally adolescents referred to substance treatment with a community comparison sample for prevalence and predictors of human immunodeficiency (HIV) virus risk behaviors of sex and injection drug use (IDU).
Methods: Structured interviews were administered at 2 time points to assess HIV risk among a clinical sample of adolescents in substance treatment and in a demographically matched community sample. The samples were followed for an mean of 7.4 years. Subjects were asked about HIV risk behaviors. Statistical procedures included chi-square tests, independent t-tests and multiple logistic regressions that controlled for baseline age, race and sex.
Results: At baseline, the clinical sample ($N=402$; mean age=15.7 years) averaged 6.2 lifetime sexual partners compared to 1.2 for the comparison sample ($N=219$) and did not always use protection 57.5% of the time (compared to 28.4%). At follow-up, the clinical sample ($N=261$) averaged 18.6 lifetime sexual partners (compared to 7.5 for the comparison group, $N=130$); 75% reported not always using protection (compared to 51%); and 18.8% reported a lifetime history of IDU (compared to 0%). The clinical sample had significantly higher HIV risk than the comparison sample at baseline and follow-up. For the clinical sample, the number of baseline conduct disorder symptoms predicted HIV risk behaviors at follow-up.
Conclusions: Adolescents in substance treatment have significantly greater HIV risk at baseline and follow-up than a demographically matched comparison sample. In addition, nearly one fifth of adolescents in substance treatment reported IDU at follow-up. Effective HIV prevention is needed for adolescents in substance treatment, especially for teens with co-occurring conduct disorder.
Financial Support: Funding: DA021913, DA011015, DA012845

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NICOTINE REINFORCEMENT BEFORE AND AFTER 72-H SMOKING ABSTINENCE IN SMOKERS WITH SCHIZOPHRENIA.

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Aims: Current smoking treatments are relatively ineffective in smokers with schizophrenia (SWS). One factor that may contribute to their high relapse rates is that SWS may experience stronger reinforcing effects of nicotine following a period of abstinence than smokers without psychiatric illness (CON). If so, then a smoking lapse (any smoking following a period of abstinence) may be more likely to lead to smoking relapse in SWS. In this study we are using high-value abstinence-contingent incentives to experimentally control smoking abstinence in SWS and CON in order to compare the reinforcing effects of nicotine in these groups before and after abstinence.
Methods: In a pre-abstinence session, participants undergo a preference task in which they first sample nicotine and denicotinized cigarette puffs under double-blind conditions and then make up to 16 choices between them. Participants then return to the laboratory twice daily over the next 72 h to provide breath CO samples and receive reinforcement for abstinence (CO ≤ 4 ppm). At the end of the abstinence period, the preference task is repeated.
Results: Results from 8 SWS and 8 CON indicate that the groups are matched on age (M = 44 yrs), gender (56% male) and number of cigarettes smoked per day (M = 21.8). Breath CO levels average 39 ppm at baseline, 18 ppm after 5-h abstinence and ≤ 4 ppm at each session thereafter, indicating the effectiveness of the contingent incentives. Percent nicotine choices in SWS are 58.6 ± 16.3% (M ± SEM) pre-abstinence and 75.0 ± 12.4% post-abstinence; in CON, percent nicotine choices are 86.7 ± 6.6% pre-abstinence and 66.4 ± 14.3% post-abstinence; this Group x Time interaction approaches significance with a large effect size (p = 0.13; eta-squared = 0.18). Ratings of the satisfaction and pleasantness of the puffs are similar across groups and do not change pre- to post-abstinence.
Conclusions: These preliminary results suggest that the reinforcing effects of nicotine may increase in SWS after a period of abstinence. If so, this may contribute to low smoking cessation rates in these smokers.
Financial Support: NIDA R21DA026829 (JWT)

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ABUSE LIABILITY INDICES ACROSS REPEATED ALFENTANIL EXPOSURES IN HEALTHY NORMALS.

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Aims: Alfentanil, a short-acting mu opioid receptor agonist, is known to have abuse potential in drug abusing volunteers. There are few data on whether repeated intermittent opioid exposures enhance abuse potential over time in non drug-abusing healthy normals.
Methods: Data were collected during a double-blind, placebo controlled study of opioid induced hyperalgesia. Healthy non drug-abusing male volunteers (N=8) received intramuscular alfentanil (15 mcg/kg) injections in 8 experimental sessions spaced 3-4 days apart. During each 480-minute session, subjective and physiological drug effects were assessed and plasma samples collected for alfentanil blood level analyses by high-performance liquid chromatography and mass spectrometry. To look for changes in abuse liability indices across sessions, repeated measures regression analyses were performed on visual analog scale (VAS) ratings of liking, drug effects, good effects, bad effects, sick, and high.
Results: Volunteers were 75% Caucasian, had a mean age of 35 years (+/-13.9) and body mass index (BMI) of 27 (+/-2.8). Peak VAS ratings occurred on average at 30 minutes after injection; mean alfentanil plasma concentration at this time point was 15.6 ng/ml (range 1.3-38). There were no differences in peak VAS ratings of liking (F=.4; p=.89), drug effects (F=1.3; p=.27), good effects (F=.94; p=.49), bad effects (F=1.1, p=.39), sick (F=.59, p=.76) and high (F=.27; p=.96) across the course of the 8 sessions. After controlling for alfentanil plasma concentration, these findings remained the same. Additionally, the average slopes of the regression lines fit to each peak VAS were all negative except for bad effects (slope=.64).
Conclusions: Abuse liability indices do not appear to increase with repeated exposure to the potent mu opioid receptor agonist alfentanil. Intermittent exposure to opioid receptor agonists over relatively short periods of time appear to be safe and not to expose subjects to enhanced abuse risk.
Financial Support: 5T32 DA07209, 1K24 DA023186.

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EFFICACY OF ANTIDEPRESSANTS IN COCAINE, IMPLICATIONS OF COMORBID DEPRESSION: SYSTEMATIC REVIEW AND META-ANALYSIS.

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Aims: To study the efficacy of antidepressant drugs in subjects with cocaine dependence with and without comorbid depression.
Methods: A systematic review and meta-analysis according to the methodology developed by the Cochrane Collaboration based on randomized controlled trials (RCTs) comparing antidepressants with placebo. A systematic search was carried out in Medline (1966-April 2010), Embase and Cochrane library. The abstracts were revised to select the eligible publications. Two outcome measures: cocaine use, measured by positive urine controls, and improvemente in depressive symptoms were analysed.
Results: Seven RCTs were included. Antidepressants evaluated: fluoxetine, desipramine, imipramine and nefazodone. Studies did not support the efficacy of antidepressant drugs for cocaine dependence, with the exception of data reported with some significant results favouring desipramine. In the condition of cocaine abuse with comorbid depression, antidepressant medication failed to produce a significant decrease in cocaine consumption, but there were an effect in the improvement in depressive symptoms.
Conclusions: Although antidepressants are commonly used in cocaine dependence, more studies are needed to confirm its usefulness. SSRIs do not seem to offer significant advantages compared with tricyclic drugs. The use of antidepressants in cocaine dependence with comorbid depression needs more studies in well-defined samples, adequate doses and duration of treatment to be really conclusive.
Financial Support: Fondo de Investigación Sanitaria, Instituto Carlos III (ISCIII: GO3/184, 06/0001/1009).

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BEHAVIORAL, BIOCHEMICAL, AND MOLECULAR INDICES OF NICOTINE WITHDRAWAL: DIFFERENTIAL IMPACT OF SEX ON STRESS-RELATED MARKERS.

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Aims: Clinical reports have suggested that during smoking abstinence, females display negative mood states, such as anxiety, that are higher relative to men. The possibility exists that intense stress produced by nicotine withdrawal may enhance the susceptibility to tobacco abuse in female versus male smokers. The present study compared anxiety-like behaviors, plasma corticosterone levels and changes in gene expression of corticotropin releasing factor (CRH) in various brain regions relevant to drug abuse in male and female rats. Sex differences were also examined by comparing nicotine metabolism via measures of cotinine (a nicotine metabolite).
Methods: Rats underwent sham surgery or received subcutaneous pumps that delivered nicotine (4.7 mg/kg/day). After 14 days of nicotine exposure, the pumps were removed to induce spontaneous withdrawal. Twenty-four hours later, anxiety-like behavior was assessed using elevated plus maze and open field maze procedures. After behavioral testing, blood samples were analyzed for corticosterone and cotinine levels. Coronal slices containing the NAcc, amygdala and hypothalamus were also analyzed for CRH gene expression.
Results: Female rats experiencing nicotine withdrawal displayed a significant increase in anxiety-like behaviors, plasma corticosterone levels, and an up-regulation of CRH mRNA expression in the NAcc relative to males. These findings are likely not due to sex differences in nicotine metabolism since cotinine levels between groups were not significantly different.
Conclusions: These findings suggest that intense anxiety produced by withdrawal may contribute to enhanced susceptibility to tobacco abuse in female versus male smokers.
Financial Support: This research was supported by the National Institute of Drug Abuse Grant R01DA021274. The authors appreciate funding by the Under-Represented Populations Committee (URPOP Primm-Singleton pre-doctoral travel award to attend the Annual Scientific Meeting of the CPDD.

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LONGITUDINAL PATTERNS OF SOCIAL NETWORKS OF WOMEN IN SUBSTANCE ABUSE TREATMENT.

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Aims: Establishing drug free networks is key to recovery yet is a challenge for women. Little is known about women's social networks as they transition into recovery. We examine longitudinal patterns of social network relationships of women in substance abuse treatment to identify structural, compositional and social support characteristics during and post intake.
Methods: Women (N = 206) were interviewed in 3 addiction treatment programs at one and four weeks post intake (T1 and T2). The Computerized Diagnostic Interview Schedule assessed co-occurring mental disorder and a network software program, Ego Net, elicited 25 network members (alters), social support and network connections. RM-ANCOVA was used to analyze T1 and T2 data. All findings significant at p<.05.
Results: Participants were 61% African American; mean age of 37 years. 74% were dually diagnosed (DD); 51% were dependent on alcohol, 62% on cocaine. At T1, the average social network consisted primarily of alters who were family (10.56), from the treatment program (2.49) and other friends (7.32). On average, 8.8 alters were actively using. Controlling for DD, treatment site, and stage of treatment, emotional ($F(1,196)=5.969$) and informational ($F(1,196)=6.445$) support, closeness ($F(1,196)=4.129$), density ($F(1,194)=5.218$), and number of non-using alters ($F(1,196)=8.664$) improved at T2. However, no significant improvements were found in concrete or sobriety support and number of alters used with. DD predicted lower emotional support, $F(1,196)=3.99$, and less closeness, $F(1,196)=4.57$.
Conclusions: Understanding social network change during the course of treatment can help treatment providers appreciate how social networks can be barriers or facilitators for change. Women with DD may need assistance to build and maintain supportive networks. Future research should examine social networks and post treatment outcomes.
Financial Support: Supported by:
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MENTORSHIP FOR ALCOHOL PROBLEMS.

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Aims: We conducted a Stage I pilot to develop a new intervention, Mentorship for Alcohol Problems (MAP), for individuals with alcohol use disorders in community treatment programs by pilot/feasibility testing, manual writing, training program development, and adherence/competence measure construction.
Methods: In Phase-I, 10 Mentors participated for 6 months in a piloting of MAP until 30 Mentees received MAP for 12 weeks. Behavioral and biological measures were conducted at baseline, weekly, monthly, and termination. During Phase II, 4 focus groups were held with the 40 pilot participants and 40 assessments were distributed to the participants' clinicians to evaluate satisfaction and guide the manual revisions.
Results: Of the 40 participants who entered the study, there were only 4 who dropped out yielding a 90% retention rate. We had a high 87%(208) attendance rate to weekly Mentorship Supervisory Groups throughout the Mentor's 6 month term and also a high 70%(252) attendance rate to the Mentorship Group. We assessed change in alcohol and drug use with all participants (N=40) by running random effect regression analyses which indicated that frequency of alcohol (p<.01), drug (p<.01), and both alcohol and drug (p<.01) use significantly decreased by week from baseline to week 12 for Mentees. All of the Mentors remained abstinent from alcohol and drugs with the exception of 1 Mentor. Using a likert scale from 1(not at all) to 7(a lot), participants indicated overall that they were very satisfied with MAP (M=6.25, SD=1.23, N=36) as well as clinicians (M=5.8, SD=1.8). On a likert scale rating the Mentor's adherence and competence in the delivery of MAP from 1(not at all) to 5(extensively) using the MACS, overall mean was M=4.36, SD=.83, N=30, adherence M=4.36, SD=.82, and competence M=4.36, SD=.84.
Conclusions: The piloting of MAP demonstrated high rates of patient acceptance and retention, substantial reductions of alcohol and drug use during treatment, clinician satisfaction, and good Mentor adherence to MAP guidelines.
Financial Support: This work was supported by NIAAA (R01AA016160).

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SMOKELESS TOBACCO USE AND ONSET OF CIGARETTE SMOKING: A CASE-CROSSOVER STUDY.

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Aims: Might the use of smokeless tobacco products (STP) protect against tobacco cigarette smoking (TCS) or might STP use function as a rapid trigger for TCS onset? We investigate the rapid triggering hypothesis using epidemiological evidence and the epidemiologic case-crossover design, which has the advantage of subject-as-own-control constraints on genetic and other individual-level susceptibility traits.
Methods: Data on a United States (US) nationally representative sample of 8,153 newly incident tobacco cigarette smokers are from the 2004-2007 National Surveys on Drug Use and Health. Computer assisted assessments covered months of onset of TCS and STP for newly incident smokers (i.e., within 24 months of assessment). We tested the triggering hypotheses, with a case-crossover hazard interval specified as month 't-1' prior to onset of tobacco smoking in month t, and with two alternative specifications for control intervals – namely, month 't-2' and month 't+1'.
Results: In a statistically powerful investigation of 8,153 newly-incident tobacco cigarette smokers, there is little evidence in favor of either reduced risk or excess risk associated with onset of using smokeless tobacco products. When month t-2 is specified as the control interval, the estimated relative risk (RR) is 1.0 (95% confidence interval, CI = 0.7, 1.5); the alternative month t+1 specification yielded RR = 1.5 (95% CI = 0.9, 2.3). In post-estimation exploration steps, alternative control month specifications did not alter these results. Recall bias did not appear to be important: the RR estimates did not vary appreciably when newly incident smokers were stratified by recency of assessment.
Conclusions: In the US, if the use of a smokeless tobacco product protects against onset of tobacco cigarette smoking or enhances risk of tobacco cigarette smoking, the process may well be one that evolves languorously over a relatively long span of time. Here, in research on a hypothesized rapid triggering process, the evidence is null.
Financial Support: NIDA support: T32DA021129 (JPT); K05DA15799 (JCA)

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INTERCONNECTION AMONG SUBSTANCE USE, DEPRESSION AND HIV RISK BEHAVIOR IN SUBSTANCE ABUSE TREATMENT PATIENTS.

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Aims: The NIDA Clinical Trials Network 12-site trial of rapid HIV testing/counseling in 1281 patients was a unique opportunity to examine relationships among (non-injection and injection) substance use, depression and sex risk behavior.
Methods: ACASI was used to assess past 6 month:substance use;substance use severity(DAST10);depression(QIDS);and sex risk behavior:unprotected vaginal/anal sex occasions;occasions while high/drunk;primary partner occasions; and non-primary partner occasions.Zero-inflated negative binomial analyses provided: probability of sex risk behavior; and rate of sex risk behavior (in the risk behavior subsample).
Results: Substance use types had differential effects on sex risk behavior.Problem drinking was the only substance indicator to show associations with all sex risk variables. Problem drinkers were 85% more likely to report some sex risk behavior(OR:1.85;CI:1.30-3.33), and over 4 times as likely to have sexual risk when drunk or high(OR:4.17;CI:2.70-6.67).The effects of other substances were limited to particular sex risk variables.Cocaine use was associated with higher odds of sex risk behavior(OR:1.79;CI:1.14-2.78).Marijuana use was associated with increased rate of sex risk behavior with a primary partner(IRR:1.62;CI:1.03-2.54).Opioid use was not associated with any sex risk behavior.Substance use severity was related to all sex risk variables.A 1 S.D. higher DAST10 score was associated with 33% increased likelihood of sexual risk OR:1.33;CI:1.05-1.69).Depression was associated with 24% decreased likelihood of sexual risk with a primary partner(OR:1.24;CI:1.06-1.44).
Conclusions: These results highlight the:roles of problem drinking and cocaine in sex risk behavior;utility of making distinctions between partner types and presence/absence of alcohol/drugs during sex;and need to integrate sex risk reduction into drug treatment.
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FEAR OF BEING KILLED BY AN INTIMATE PARTNER: THE IMPACT OF SUBSTANCE ABUSE.

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Aims: Among heterosexual couples, research has found an association among increases in intimate partner violence(IPV) and both men and women's use of alcohol and/or drugs (Fals-Stewart,2003; Kantor & Straus,1989). These data are consistent with our research finding, which has shown a significant relationship between batterer substance abuse and the severity of domestic violence. However, one recent study found that after controlling for men's use of alcohol, women's alcohol use was no longer significantly associated with an increase in IPV(Lipsky et al.,2005). This begs the question: do woman use in response to IPV or does IPV increase when a victim uses alcohol or drugs? Women experiencing IPV frequently develop a fear of their partner and may become afraid for their life(Olson et al.,2008). The purpose of this study is to explore whether the batterers' use of alcohol and/or drugs increases fear in their partner and if women turn to alcohol and/or drugs in response to this fear.
Methods: One hundred seventeen women were recruited from three emergency domestic violence shelters in New York City. Participants provided yes or no responses to questions regarding their male batterers' alcohol and substance abuse and their fear of being killed by their batterer, as part of the Danger Assessment(Campbell,2003). Participants also indicated whether they themselves had used alcohol and/or drugs within the past six months.
Results: A series of chi square analyses yielded significant results among batters' alcohol abuse and victims' fear ($c2(1,n=117) =6.23$ $p=.001$). Seventy-five percent of participants who described their batterer as an alcoholic believe their batterer is capable of killing them. No significant relationships were found among batters' drug use and victims' fear or victims' fear and their own use of alcohol or drugs. However, only 32% of participants who believe their partner is capable of killing them reported having used alcohol or drugs within the past six months.
Conclusions: These findings suggest that males' alcohol abuse may increase victim's fear of their partner and may further complicate mental health responses to IPV.
Financial Support: URI

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SUBLINGUAL ADMINISTRATION OF ALKS 33, A NOVEL OPIOID RECEPTOR ANTAGONIST, DOES NOT ALTER BUPRENORPHINE PHARMACOKINETICS.

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Aims: ALKS 33(ALKS33), a μ-opioid receptor antagonist with κ and δ-agonist/antagonist activity, is in development for the treatment of addictions. Buprenorphine(BUP) may be useful in the treatment of cocaine addiction if administered safely to nonusers of opiates. As part of a Phase1 study, which evaluated the ability of ALKS33 to block the μ-opioid receptor agonism of BUP, the PK of sublingual(SL) ALKS33 and co-administered BUP were investigated.
Methods: A single-center, double-blind, randomized, PBO, cross-over study in 12 opioid experienced, non-treatment seeking subjects enrolled two cohorts (n=6). Randomized dosing sequence of 3 SL administrations of study drug (ALKS33 1, 4 mg and PBO; or 8, 16 mg and PBO) coadmin with BUP (8 mg). Visits were separated by a min of 7 days. Blood samples drawn for PK analysis of ALKS33, BUP and norbuprenorphine (nBUP) predose through 24 hours post-dose. ALKS33, BUP, and nBUP concentrations were determined by LC/MS/MS. PK params were calculated using non-compartmental techniques.
Results: SL ALKS33 and BUP were rapidly absorbed, with Tmax of ~1 for both. Cmax(mean ± SD) of ALKS33(1-16mg) ranged from 1.8±0.4 - 33±15 and exposure was dose proportional (AUC∞ 12±4 - 267±90). ALKS33 conc declined in a mono-exponential fashion(t1/2 5.9 - 6.8 hr) and were measurable at 24hr (exception: 1 mg ALKS33). Cmax and AUC0-24h of BUP was similar across ALKS33 doses (range: 2.2±1.7 - 3.0±1.4; 10.8±5.9 - 15.9±5.6, respectively) compared to BUP alone(2.4±0.8 – 2.6±1.4; 12.4±2.4 – 12.9±5.4). Cmax and AUC of nBUP appeared to be slightly greater with ALKS33 coadmin.
Conclusions: ALKS33 was associated with dose dependent blockade of BUP μ-opioid agonism; coadmin of ALKS33+BUP was safe and well tolerated. ALKS33 was well absorbed following SL administration and exhibited high systemic exposure. The PK of BUP and nBUP were not impacted by co-administration of ALKS33.
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ABSENCE OF SEX DIFFERENCES RELATED TO THE NEONATAL ABSTINENCE SYNDROME AMONG INFANTS BORN TO WOMEN IN OPIOID AGONIST TREATMENT.

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Aims: Prior research suggests that male neonates are generally more vulnerable to postpartum stress factors than females. Using a unique prospective design, this study tested the hypothesis that male neonates born to opioid dependent mothers differ from female infants in terms of opioid withdrawal; specifically, in neonatal abstinence syndrome (NAS) development, severity, medication requirements and duration.
Methods: This study was a part of the Maternal Opioid Treatment: Human Experimental Research (MOTHER) study, a randomized, double-blind, double-dummy multi-center trial examining the comparative safety and efficacy of methadone and buprenorphine during pregnancy. It includes data from 131 neonates born to opioid dependent women randomized at seven sites. Sex-specific differences in birth weight, length, head circumference, NAS duration, severity and treatment parameters were assessed.
Results: Boys had a significantly higher birth weight ($p=0.027$) and head circumference ($p=0.017$) than girls; however, no significant sex-related differences were found for NAS development, severity and treatment parameters.
Conclusions: No sex differences in NAS were observed in this sample, suggesting that infant boys and girls born to opioid dependent women have similar perinatal vulnerability.
Financial Support: grants from National Institute on Drug Abuse: R01DA015778 (Brown University), R01DA15832 (Wayne State University), R01DA015764 (Johns Hopkins University), R01DA015738 (Thomas Jefferson University), R01DA015741 (University of Toronto), R01DA017513 and M01RR00095 from the General Clinical Research Center (Vanderbilt University), R01DA018410 (University of Vermont) and R01DA018417 (University of Vienna).

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CLIENT TRANSFERS AS A CONTINUITY OF CARE MEASURE.

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Aims: Treatment for substance abuse disorders often is delivered in a fragmented way that is inconsistent with the current view of addiction as a chronic disease requiring adaptive treatment.
The present study addresses the following questions:
1) What percentage of alcohol and other drug treatment admissions in California resulted in a transfer from one service to another (e.g., detox to residential, residential to outpatient)?
2) What client background characteristics are related to transfer rates?
3) Are transfers related to client outcomes?
Methods: Analyses were conducted on all admissions recorded in the California Outcomes Monitoring System-Treatment (CalOMS-Tx) from July 1, 2008, through June 30, 2009, inclusive.
Transfers were defined and identified by a SAS program if no more than 30 days passed between a discharge and an admission to a subsequent or overlapping service. Since detoxification alone does not constitute complete treatment, detox-to-detox movements were not counted as transfers to treatment.
Results: Transfers were rare, occurring after only 10% of outpatient admissions and 20% of residential admissions.
Detox-only admissions (no transfer) were common, accounting for 85% of detox admissionis, and 19% of all admissions.
Detox admissions were less likely to result in a transfer to treatment if the client admitted was male, Black/African American, homeless, not pregnant, older, reported alcohol as their primary drug, or if the client was referred from a non-coerced (e.g. non-criminal justice) source.
Over the course of a treatment episode with transfers, outcomes improved from admission to initial discharge to final discharge on self-report measures of social support, employment, drug use, and jail incarceration. However, transfers did not predict arrests recorded in administrative records.
Conclusions: Administrative data on transfers can be an informative tool to measure continuity of care and disparities in services. However, data quality issues must be considered prior to widespread use.
Financial Support: This research was supported by a contract from the Californa Department of Alcohol and Drug Programs.

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THE IMPACT OF METHAMPHETAMINE USE ON OUTCOMES IN HERPES SIMPLEX VIRUS TYPE 2 DISEASE AND IMMUNE RESPONSE.

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Aims: Methamphetamine (METH) use is associated with increased risk for acquiring sexually transmitted infections (STIs). There is increasing evidence that this association is not based solely on behavioral risk factors. However, the impact of METH use during exposure to an STI has not been explored. We hypothesized that METH enhances the disease of an important STI, herpes simplex virus type 2 (HSV-2), by altering the host immune response to infection.
Methods: C57BL6 mice were subcutaneously injected with METH (10 mg/kg) or saline once daily for 5 days, with intravaginal HSV-2 inoculation on the 3rd day of treatment. We examined the onset of clinical signs of disease (CSD) and virus translocation to sensory ganglia (n=20). We also performed cytokine and ELISpot analysis to examine IFNγ levels in the genital tract and iliac lymph nodes [iLN] (n=10).
Results: METH treatment resulted in earlier onset of mean CSD (4.6 days) vs. controls (5.6 days; p<.01, Student's t-test). This corresponded with increased viral DNA in the ganglia (374 vs 133 HSV genome equivalents/10^4cells). Additionally, METH significantly increased IFNγ levels in the genital tract early post-infection [pi] (39.5 vs. 29.4 pg/mL; p<.05), but significantly reduced IFNγ secreting cells in the genital tract later pi [626 vs. 9872 spot forming cells (SFC); p<.01]. Interestingly, this late infection in METH treated animals was associated with increased IFNγ secreting cells in the iLN (2911 vs. 1321 SFC, p<.05).
Conclusions: METH alters HSV-2 disease and immune responses in the genital tract. The unexpected increase in IFNγ in the genital tract early pi is of particular interest because of its role in viral clearance. This may indicate that there is an effect of METH on IFNγ receptor function which may also be reflected in the later IFNγ levels in the genital tract and iLN. These findings have important public health implications and may be more broadly applicable to other important STI's such as HIV.
Financial Support: Supported by the SCVD Fellowship and Vale-Asche/McLaughlin Fellowship

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EVOLUTIONARY IMPLICATIONS FOR ANIMAL MODELS IN ADDICTION RESEARCH.

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Aims: Human diseases of addiction are recognized as genetically complex, polygenic disorders with great allelic heterogeneity. Yet historically, animal models have first been driven by practical concerns: reproduction rates, husbandry costs, amenability to manipulation. This gulf between the tools available to researchers and the reality of the disease has resulted in incomplete understandings and difficulties in translating basic research to the bedside. Recent studies have focused on developing animal models with validated phenotypes directly relatable to human disease and with similar underlying causes; genetic, epigenetic, or environmental. This has been fueled in part by a transition to a post-genomic era where genetic information is more widespread and the molecular etiology of disease is more apparent. Using evolutionary and comparative genetic approaches we can better facilitate translational research in addiction.
Results: In comparing across the genome, we have demonstrated that genes associated with addiction disorders show higher conservation across mammals than those associated with other neuropsychiatric disorders, yet there are specific and important caveats. A major drug target of amphetamines, TAAR1, is absent in canids. The opioidergic system shows evidence for selection in the apes; the MAOA gene has experienced positive selection in humans. Recurrent variation among primate species in numerous genes, including SERT, DAT, MAOA, OPRM1, and others, has been associated with numerous addiction pathologies.
Conclusions: As animal models are developed with genetic and molecular etiologies that more closely mimic human disease states, new considerations are arising regarding differences in protein function between species and their effects on the translational validity of findings. By more formally addressing these questions we can generate better animal models and produce more immediately translational results and better understand the strengths and limitations of our previous studies.
Financial Support: This work was supported by: AA019688 (EJV); MH077995 (GMM); DA025697 (GMM) and RR00168 (NEPRC).

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KNOWLEDGE OF INFORMED CONSENT INCREASES PROPORTIONATELY WITH EDUCATION.

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Aims: Informed consent is the ethical foundation of modern medical and psychiatric care. As treatments for patients with addictions evolve and new therapies are introduced, it is unclear whether individuals administering addiction treatment fully understand informed consent practices. The aim was to investigate variables associated with addiction treatment professionals' knowledge of informed consent.
Methods: Licensed and unlicensed addiction treatment professionals (N=805), practicing in Community Treatment Programs within the National Institute on Drug Abuse Clinical Trials Network responded anonymously to an internet based survey investigating their knowledge of informed consent and were compensated $50. Survey questions were derived from previous surveys, ethical policies, and published literature. Analyses focused on determining relationships between participant knowledge of informed consent (14 questions) and individual attributes such as education and training.
Results: Comparison amongst mean scores obtained on participant knowledge of informed consent and personal attributes was performed. The results showed that participants with a higher level of education scored significantly better than participants with a lower level of education ($p < 0.05$). Relationships between knowledge of informed consent and licensure, age, job title and other attributes were not significant.
Conclusions: Individuals with higher levels of education had greater knowledge of informed consent practices than individuals with a lower education possibly due to having more formal education on ethical topics related to informed consent. These results do not reflect care administered or patient outcome success, but may indicate a need for the development and implementation of universal training courses on ethics and informed consent practices in addiction treatment programs.
Financial Support: National Institute on Drug Abuse

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DOSE EFFECTS OF ORAL THC IN HEAVY CANNABIS USERS.

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Aims: Assess the dose effects of oral THC on withdrawal, cognitive performance, and the effects of acute smoked cannabis in daily cannabis users.
Methods: Daily cannabis users (N=7) were orally administered 0, 10, 20, and 40mg THC tid on 5 consecutive days in a counterbalanced order on a residential unit. THC administration periods were separated by 9 days of ad-lib cannabis use. Subjective and physiological measures were obtained daily. On the last day of each study period, participants completed cognitive performance testing and were administered 5 puffs of smoked cannabis (5.9% THC). Repeated measures analyses were conducted to detect differences based on cannabis use (ad-lib vs. no smoking) and oral THC dose conditions.
Results: Compared with placebo, 40mg THC significantly attenuated subjective ratings of cannabis withdrawal including loss of appetite, nausea, irritability, muscle spasms/aches, chills, headaches, and stomach pains. THC did not suppress withdrawal-induced sleep disturbance or craving for cannabis. No significant side effects or cognitive performance impairing effects were observed at any dose of THC. Participants rated the subjective effects of smoked cannabis (5 puffs) as being greater while maintained on 40mg THC compared with placebo and lower doses.
Conclusions: A dose-effect of oral THC was observed in heavy cannabis users such that 40mg tid, but not lower doses, suppressed several cannabis withdrawal symptoms without inducing side effects or cognitive impairment. Withdrawal suppression may be therapeutically beneficial to individuals trying to stop cannabis use. Interestingly, the subjective effects of smoked cannabis were enhanced rather than dampened while receiving 40 mg THC, an effect that may be counterproductive for relapse prevention. It is possible that higher doses of oral THC would dampen subjective effects of smoked cannabis while maintaining the benefits of withdrawal suppression, a pattern that would better support therapeutic utility. While relief of withdrawal may be sufficient to warrant clinical use, additional research is needed to determine the overall utility of oral THC as a treatment for marijuana use disorders.
Financial Support: NIDA Grant DA025044

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ABUSE LIABILITY ASSESSMENT OF ELECTRONIC CIGARETTES IN CIGARETTE SMOKERS.

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Aims: Electronic cigarettes (ECs) are marketed to smokers as reduced exposure products and are widely available even though little is known about their behavioral or physiological effects. In an ongoing investigation, the nicotine delivery profile, and subjective, cardiovascular, and reinforcing effects of the "Vapor King" EC are being examined.
Methods: Ten participants (5 women, 2 Caucasian) that smoke >15 cigarettes per day have completed this within-subject, four session protocol. The first session is a sampling session that involves six 10-puff bouts (30s IPI) with the "Vapor King" EC (18 mg) at 30 minute intervals. During the sampling session, blood plasma is collected to be analyzed for nicotine, heart rate and blood pressure are monitored, and subjective effect questionnaires are completed. During the remaining three sessions, participants make choices on a multiple-choice questionnaire between 10 puffs from the EC or varying amounts of money ($0.01, 0.02, 0.04, 0.08, 0.16, 0.32, 0.64, 1.28, 2.56, 5.12), 10 puffs from the EC or a varying number of puffs from their own brand (1, 2, 3, 4, 5, 6, 7, 8, 9, 10 puffs), or 10 puffs from their own brand and varying amounts of money. The choice questionnaire is completed six times at 30-min intervals, and one choice is randomly reinforced at each trial.
Results: Interim findings suggest that 60 puffs from the "Vapor King" EC results in nicotine delivery (mean peak plasma nicotine: 6.5 ng/ml [N=6]) as well as tobacco abstinence symptom suppression (e.g. decreased ratings of "craving") and increased ratings of product acceptability (e.g. "satisfying"). On the multiple-choice questionnaire, participants chose to receive 10 puffs from the "Vapor King" EC instead of an average of $0.55 or 2.4 own brand puffs and chose 10 puffs from their own brand over an average of $0.95.
Conclusions: Findings indicate that, relative to traditional tobacco cigarettes, ECs may have a lower potential for abuse in current cigarette smokers. While these results address some effects of ECs during a short-term laboratory study, risks associated with long-term use of ECs remain uncertain.
Financial Support: R01CA103827, R01CA120142, T32DA007027-34.

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DRUG USE AMONG POOR AFRICAN-AMERICAN VETERANS: A SECONDARY ANALYSIS OF DATA FROM THE NATIONAL SURVEY ON DRUG USE AND HEALTH.

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Aims: Much information is coming to light regarding the struggles of returning veterans to reintegrate into civilian life. This study expands that literature by explicitly looking at the experiences of poor predominantly African American veterans returning to the inner-city.
Methods: This paper presents secondary analysis of NSDUH data that compares poor African American veterans' drug use and mental health to the levels in the general population, as well as among poor African Americans who have not served in the military, and among other veteran population. This analysis is part of a larger project that includes a 5-year panel study of poor predominantly African American veterans returning to the inner-city.
Results: Our findings expand upon a series of recent SAMHSA reports, some of the key findings of which include the following: Veterans are somewhat more likely to use substances than general population; they had higher prevalence rates of past month marijuana use (3.5 vs. 3.0%) and past month heavy use of alcohol (7.5 vs. 6.5%). The analysis of younger cohorts (20-39 years) demonstrated that female veterans are significantly less likely to engage in drinking, smoking, and using drugs than men despite the fact that they are twice as likely to experience major depressive episodes (MDE; 17 vs. 8%) and serious psychological distress (SPD; 15 vs. 7%). In line with our expectations, African American veterans have the highest rate of MDE and veterans from poor families are more likely to experience SPD and substance use disorder.
Conclusions: A high proportion of returning veterans have been experiencing drug and alcohol problems, psychological distress, and civilian reintegration problems. The analyses planned should yield insights that will lead to improvements in outreach and treatment programs for the predominantly African Americans veterans returning to the inner-city, who face particularly high risks and more complex problems than other veterans.
Financial Support: The Veteran Reintegration, Mental Health, and Substance Abuse in the Inner-City Project (#R01 AA020178) is supported by NIAAA.

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PREVALENCE, FREQUENCY, CORRELATES AND OUTCOMES OF BENZODIAZEPINE USE AMONG PATIENTS IN METHADONE MAINTENANCE TREATMENT.

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Aims: To evaluate prevalence and frequency of benzodiazepine (BZD) use and to explore differences in the demographics, mental health functioning, and treatment outcomes of regular (BZD positive tests>= 30%), occasional (BZD positive tests< 30%) and non-BZD users among methadone maintenance treatment (MMT) patients.
Methods: We reviewed electronic charts containing demographics, urine toxicology test (UTOX) results, and admission BASIS-24 scores (reflecting the mental health functioning) of a cohort of patients initiating treatment in four outpatient MMT clinics in New Haven, CT between July 1, 2007 and June 30, 2008. Data spanning 1 year following admission from 415 patients who had stayed in treatment for at least 3 months and had at least 3 UTOXs were included in the analysis.
Results: 190/415 participants (45.8%) had evidence of at least one positive UTOX for BZD during treatment. Of these, 102/415 (24.6%) were occasional and 88/415 (21.2%) were regular BZD users. Both regular and occasional BZD use were significantly more prevalent among Caucasians. Elevated depression, self-harm, and overall dysfunction scores on BASIS-24 at baseline were associated with occasional BZD use during treatment ($p<.05$ for all). Both regular and occasional BZD use were associated with higher methadone dosage ($p<.05$). Neither occasional nor regular BZD use was associated with treatment retention ($p=.420$), take-home status ($p=.093$), opiate ($p=.445$), or cocaine ($p=.952$) use during treatment. However, cocaine and opiate use were positively correlated with each other ($p<.05$) and with lower treatment retention ($p<.05$), and lower rates of take-home privileges ($p<.05$).
Conclusions: While BZD use was common in our sample, unlike the use of cocaine and opiates during MMT, BZD use was not associated with adverse treatment outcomes. Patients presenting with higher mental health dysfunction at treatment entry used BZD at higher rates during treatment, but available data were not able to differentiate between medically-prescribed BZD use and non-medically prescribed or inappropriate BZD abuse.
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ADOLESCENT AMPHETAMINE EXPOSURE ALTERS PERFORMANCE IN MEDIAL PREFRONTAL CORTEX SENSITIVE TASKS.

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Aims: Drug use typically begins in adolescence, which is a period of heightened vulnerability due to ongoing neurobiological development. Previously, our lab has shown that amphetamine (AMPH)-induced deficits in a medial prefrontal cortex (mPFC)-sensitive working memory task are greater in rats given the drug during adolescence rather than adulthood. Recently, we examined if AMPH exposure during adolescence would alter impulse control in adulthood by training rats in a differential reinforcement of low rates (DRL) task.
Methods: Male Sprague-Dawley rats were injected (i.p.) with saline or 3 mg/kg AMPH every other day from postnatal day (P) 27-45 (10 injections total). Starting on P125, they were trained to lever press for food pellets on an FR1 followed by a DRL5 schedule. For the latter, responses were reinforced only when they were separated by ≥ 5 sec. Rats were then moved to longer delays of up to 30 sec (DRL30), where baseline performance was established for 30 sessions. Lastly, rats were given saline or AMPH (0.25-1 mg/kg) 10 min prior to daily sessions.
Results: AMPH exposure during adolescence increased perseverative responding following reinforcement. Response efficiency (reinforcements/lever presses x 100) was similar in saline- and AMPH-exposed rats. Furthermore, AMPH injection prior to testing on DRL30 dose-dependently reduced impulse control in both groups.
Conclusions: Our results suggest that AMPH exposure during adolescence produces modest, though long-lasting deficits in response inhibition. Because this behavior is sensitive to disruptions in mPFC function, we are undertaking follow-up studies to determine if these effects are also evident in an mPFC-sensitive, cognitive flexibility task (attentional set-shifting). In these studies, we utilize a group of adult-exposed rats to determine if observed deficits are dependent on the age of exposure. Taken together, our studies suggest that the developing mPFC is especially vulnerable to AMPH-induced plasticity and the long-lasting consequences on cognition.
Financial Support: Arnold O. Beckman Award, UIUC

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PRACTICING RELAPSE PREVENTION IN ARTIFICIAL REALITY ENVIRONMENTS: USING COMPUTER SIMULATIONS AS AN ADJUNCT FOR TREATMENT IN VETERANS WITH ALCOHOL USE DISORDER.

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Aims: The aim of this study was to develop and test a computerized role-playing simulation designed to teach and allow for practice of relapse prevention skills in individuals with alcohol use disorders.
Methods: A computerized game simulation was developed in which participants would play a character recovering from alcohol dependence. Participants chose daily activities for this character (e.g. go to movies, AA meetings, therapy, etc.) in an attempt to keep the character from relapsing. Built within the interface were 4 interactive mini-games that allowed participants to plan their travel routes around high risk areas, practice drink refusal skills, practice removing alcohol from the home, and attend therapy sessions that reviewed various aspects of relapse prevention skills. Participants were 43 male veterans enrolled in an intensive substance abuse treatment program who were randomized to either play the game or to view power point slides that reviewed information related to relapse prevention. During 8 research visits over a 16-week period, patients completed questionnaires and either played the game for an hour or were allowed to view the slides for up to an hour. The primary dependent variable was rate of relapse, with secondary dependent variables consisting of ratings on the Obsessive Compulsive Drinking Scale (OCDS), the Alcohol Urge Questionnaire (AUQ), and the Task Specific Self Efficacy Scale (TSSE).
Results: Groups did not differ with respects to rates of relapse. However, GEE analyses revealed that those within the game condition showed greater reductions in OCDS ratings, lower ratings of craving, and higher ratings of self-efficacy.
Conclusions: Game simulations designed to practice relapse prevention skills may reduce thoughts and desires related to alcohol use, and may increase self-efficacy with respects to using relapse prevention skills.
Financial Support: Robert Wood Johnson Foundation

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ASSESSMENT OF INDIVIDUAL DIFFERENCES IN THE REWARDING AND AVERSIVE EFFECTS OF 10 MG/KG MORPHINE.

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Aims: Drugs of abuse produce both rewarding and aversive effects. Recently, we examined the relationship between these effects in individual subjects receiving 5 mg/kg morphine and found no relationship between the ability of morphine to condition a place preference and its ability to condition a taste aversion. The present study further examined the individual differences in the rewarding and aversive effects of morphine at the dose of 10 mg/kg using a combined conditioned taste aversion/conditioned place preference procedure.
Methods: Male Sprague-Dawley rats (n=25) were given 20-min access to saccharin (0.1%) followed by a subcutaneous injection of morphine (10 mg/kg) or drug vehicle and placed in the initially non-preferred compartment of a CPP apparatus for 30 min. On the next day, the subjects received 20-min access to water followed by an injection of vehicle and placed in their preferred CPP compartment. This cycle was repeated three times. Subjects were tested for their acquisition of place preference following each conditioning cycle and received a final taste aversion test following place preference conditioning.
Results: After one conditioning cycle, Paired Samples t-test showed that the subjects receiving morphine readily acquired a conditioned taste aversion ($p's < 0.001$) but not a conditioned place preference ($p's > 0.05$). After three conditioning cycles, morphine-treated animals continued to display a taste aversion and spent more time on the drug-paired side (i.e., they acquired place preference). Although both effects were conditioned, there was no relationship between the strength of taste aversion and the strength of place preference on any trial (Pearson Correlation $r's \leq 0.021$, $p's \geq 0.931$).
Conclusions: Although morphine has both rewarding and aversive effects (as assessed by the conditioned place preference and conditioned taste aversion designs, respectively), these effects appear unrelated, suggesting that these two affective properties of morphine are mediated by different mechanisms.
Financial Support: Supported by a grant from the Mellon Foundation to AV and ALR.

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SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL CANNABINOID ANTAGONISTS.

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Aims: Recent studies in our laboratories have shown that a series of 4-carboalkyl-1,5-diaryl-1,2,3-triazoles exhibit potent affinity (nM) for CB receptors in rat brain tissue. The aim of the present study was to synthesize and evaluate the preclinical biological activity of novel 1,5-diaryl-1,2,3-triazole derivatives.
Methods: A series of 1,5-diaryl-1,2,3-triazoles were prepared via a [3+2] cycloaddition reaction. The CB1 binding affinity was determined by inhibition of [^{3}H]SR141716 binding. High affinity compounds were evaluated in vivo to determine their effects alone and in combination with WIN 55, 212-2 on locomotor activity in rats.
Results: The 4-carbopropoxy-1,5-diaryl-1,2,3-triazole (HS57-4) exhibited potent CB1 receptor affinity (K_i = 5 nM). In addition, HS57-4 (3 mg/kg) antagonized the effects of WIN 55,212-2 on locomotor activity in rats. Alone, HS57-4 exhibited no locomotor stimulant activity, unlike SR141716 which exhibited locomotor stimulation at similar doses.
Conclusions: These preliminary studies indicate that the 1,5-diaryl-1,2,3-triazole molecular scaffold is viable for the development of potent CB1 receptor ligands. Moreover, the propyl ester HS57-4 was found to exhibit a novel cannabinoid neutral antagonist profile.
Financial Support: NIDA R01 DA023916

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FURTHER VALIDATION OF "NEUROCHEMICAL FINGERPRINTING" TO CHARACTERIZE DRUGS WITH DIFFERENT PRESYNAPTIC DOPAMINERGIC MECHANISMS: COMPARISON WITH IN VIVO MICRODIALYSIS.

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Aims: We have shown that various indirect dopamine (DA) mimetic drugs have specific "neurochemical fingerprints" (unique patterns of changes of DA metabolites) in mouse striatum (Heal et al, 2009). In the present study, we have compared the effects of d-amphetamine (d-AMP) on striatal DA and its metabolites using neurochemical fingerprinting and in vivo microdialysis in freely-moving mice.
Methods: Male C57/BL6 mice (n=6-18 neurochemistry; n=3 microdialysis) were injected ip with d-AMP (3mg/kg) or saline. For neurochemical fingerprinting, they were killed at 60 min, and striatal DA, DOPAC and HVA determined simultaneously by HPLC/amperometric electrochemical detection (ECD) (Cheetham et al, 1996) and 3 MT by HPLC/coulometric ECD (Heal et al, 1990). Microdialysis probes (2.0mm, CMA) were inserted into striatum via guide cannulae (coordinates: AP= +0.7; ML= -1.7mm; V= 2.0; Paxinos & Franklin, 2001), 24h before determining the effects d AMP (3mg/kg ip) on efflux of DA, DOPAC, HVA and 3 MT using an Alexys HPLC/ECD system.
Results: All data are reported as percentages of control and all changes were significant ($p<0.05$). Neurochemical fingerprinting showed that d AMP did not alter striatal DA content, but decreased DOPAC (30%) and HVA (47%). Striatal 3 MT (148%), DA/DOPAC (321%) and DA/HVA (198%) ratios were increased. Microdialysis data showed that maximum effects of d AMP decreased DOPAC (21± 5%) and HVA (63±2%). DA (1225±299%) was increased, as were ratios of DA/DOPAC (4029±1936%) and DA/HVA (1400±290%). Dialysate 3 MT was below the level of detection.
Conclusions: In summary, the striatal neurochemical fingerprint of d AMP, determined ex vivo, is consistent with its effects on DA and its major metabolites determined by in vivo microdialysis. These results provide further evidence that neurochemical fingerprinting is a rapid and elegant technique that can be used to identify the presynaptic mechanisms of novel dopaminergic compounds.
Financial Support: RenaSci Consultancy

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STRESS-INDUCED REINSTATEMENT OF CONDITIONED PLACE PREFERENCE INDUCED BY MDMA OR COCAINE IN ADOLESCENT MICE.

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Aims: Aim: MDMA abuse is often encountered in adolescent and young adult cohorts, compared to older adults. The present study aimed to assess the role of stress in inducing reinstatement of MDMA- or cocaine-induced CPP in adolescent mice.
Methods: Methods: Forty adolescent mice (PND 28) were conditioned with 25 mg/kg of cocaine or 10 mg/kg of MDMA in a CPP paradigm. After extinction of the preference, all mice were restrained in a cylindrical glass tube for 15 minutes. Half of the conditioned animals performed the reinstatement test immediately after the restraint procedure ("immediate" group), whereas the other half performed it 15 minutes later ("delayed" group). We have previously reported that this kind of stress induced an increase in corticosterone levels that peaks immediately after the end of retraint. All procedures involving the mice and their care complied with national, regional and local laws and regulations, and with European Community Council Directives (86/609/EEC, 24 November 1986).
Results: Results: Reinstatement of cocaine-induced CPP was induced both in the "immediate" and "delayed" test groups. By contrast, MDMA-induced CPP was reinstated only in the "immediate" testing group.
Conclusions: Conclusions: To our knowledge, this is the first study to report that physical stress can reinstate MDMA -induced CPP, in this case in adolescent mice. In addition, our results support previous findings showing that stressors can also reinstate cocaine-induced CPP.
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MARIJUANA USERS' SOCIAL NETWORKS, MARIJUANA USE, AND PROBLEMS.

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Aims: Marijuana (MJ) users often pool their MJ and share it with friends. Having MJ-using friends in young adulthood has been shown to distinguish heavy versus light MJ users. Thus, one's social network can promote MJ use, possibly leading to MJ problems and/or dependence. Our aim was to test the relation between MJ users' social networks and their MJ use and problems. To test this aim, we used a sample of young adults (age 18-30 years; M = 23 years) who were regular (i.e., once/week) MJ users.
Methods: The sample (N = 76) was 76% male, 66% European American, 50% students, and 91% low income. Participants completed questionnaires on variables of interest. For MJ use, they estimated the number of "average-sized" joints they smoked or if they used other methods (e.g., bowls), the number of joints they could have rolled. MJ problems were measured using the Marijuana Problem Index. Social network variables were derived from reports on the substance use of up to 10 people with whom they used MJ.
Results: Participants used MJ weekly (41%) or daily (59%). They used MJ in bowls/bongs (60%), blunts (34%), or joints (5%) and smoked with others (86%). On average, they smoked 15.4 joints/week (range 2-52; SD = 11.1). About half (51%) met DSM-IV criteria for current MJ dependence. On average, they reported 7.1 social network members (range 3-10; SD = 2.2), typically friends similar in demographics and MJ use.
In hierarchical regressions, social network variables were used to predict weekly MJ use and MJ problems. Controlling for participant demographics and MJ dependence, the percentage of MJ-dependent social network members: a) predicted ($p < .05$) participants' weekly MJ use (total variance = 29%); and b) was marginally related ($p = .08$) to MJ problems (total variance = 23%).
Conclusions: Young-adult MJ users who smoke with friends who have MJ-use disorders report greater MJ use and more MJ problems. MJ use "buddies" may place them at risk for excessive MJ use and related problems or dependence.
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RELATIONSHIP OF BINGE DRINKING TO DRUG USE AMONG NIGHTTIME WEEKEND DRIVERS.

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Aims: This study is based on a sample of 4,640 weekend nighttime drivers interviewed in the 2007 National Roadside Survey, who reported alcohol use in the past year and provided breath samples for determining blood alcohol concentration (BAC) and oral fluid samples for drug analysis. Two measures of high-risk drinking—reported monthly binge drinking and an illegal .08 BAC at the time of driving—were related to three measures of illicit drug use: self-reports of marijuana and cocaine use and the presence of any illegal drug in the oral fluid test while driving.
Methods: This is a secondary analysis of self-report and chemical test data from interviews with 4640 drivers stopped at the roadside and interviewed from 10 p.m. to midnight and 1 to 3 a.m. on Fridays and Saturdays at 300 locations within the 48 contiguous states between June and July 2007. Police directed a random sample of motorist into an off-road area where they were approached to participate in the voluntary, anonymous survey. The key data collected for this study were self-reported binge drinking and drug use and quantitative measures of blood alcohol and drug concentrations in oral fluid and blood. Regression analysis of covariates (age, gender, ethnicity, educational attainment, employment, driving mileage, time of night, previous arrest, and other relevant variables) were used to establish the relationship between reported binge drinking and detection of illegal drugs.
Results: Drivers reporting monthly binge drinking in the last year were 2.5 times more likely than nonbinge drinkers to have an illegal substance detected in either their oral fluid or blood samples, and drivers who had been binge drinking on the night of the survey, as indicated by having a BAC of .08 or greater, were 3.8 times more likely to be positive for an illegal drug.
Conclusions: Binge drinkers are more likely that the average driver who drinks to be using drugs on the highway.
Financial Support: NHTSA, NIAAA

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AN ANALYSIS OF COUNSELING SESSIONS ATTENDED BY OPIOID-DEPENDENT PARTICIPANTS IN A MULTICENTER TRIAL OF BUPRENORPHINE/NALOXONE.

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Aims: An open-label, multicenter office-based trial of buprenorphine/naloxone for the treatment of opioid dependence was conducted in 38 physicians' offices and clinics
Methods: Five hundred eighty-two opioid-dependent participants were enrolled in the study. The protocol stipulated that participants could receive up to 26 counseling sessions that would be reimbursed by NIDA/VA funding. Counseling could be provided by any one or more of the following sources: an on-site medical assistant (trained to administer relapse prevention counseling), a drug counselor (on-site or off-site), or Narcotics Anonymous. The following types of counseling were recorded: individual counseling, group counseling, AIDS counseling, or "other".
Results: Compared to non-completers (n=393), completers (n=189) received more individual plus any other types of counseling (51% v. 27%; p<0.0001). 95% of the completers received some type of counseling whereas only 71% of the non-completers received some type of counseling (p<.0.0001).
Conclusions: Completers and non-completers also differed on the number of counseling sessions attended of each counseling type (all ps<.001).

Table 1: Mean number of counseling sessions

Type of Counseling	Completers	Non-Completers	X2	p
Individual (I)	15.5	4.8	157	<0.0001
Group (G)	27.4	9.3	62	<0.0001
AIDS (A)	0.1	0.02	63	<0.0001
Other	2.2	1.1	11	<0.0006
I + G	42.9	14.1	118	<0.0001
I + G +A	43	14.2	118	<0.0001

Table 2: Median number of counseling sessions

Type of Counseling	Completers	Non-Completers
Individual (I)	14	1
Group (G)	4	0
I + G	24	4

Key word: buprenorphine/naloxone
Financial Support: Trial was funded by NIDA.

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ASSESSMENT OF THE EASE WITH WHICH PRESCRIPTION OPIOID ABUSERS PREPARE A TRF VERSUS A NON-TRF FOR ABUSE.

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Aims: Tamper resistant formulations of prescription opioids (TRF) have been developed to deter abuse. The purpose of the present studies was to examine whether experienced prescription opioid abusers were able to prepare a tapentadol TRF (50 mg, 250 mg) for abuse, utilizing an OxyContin® tablet (40 mg) as a positive control.

Methods: Participants received 3 tablets in random order and were instructed to prepare them for intranasal (Study 1) or intravenous use (Study 2) using tools/solutions of their choice. No drug was administered.

Results: Study 1. All 25 participants were able to render the OxyContin® into a powder they were willing to snort, compared to 25% and 16% for the TRF 50 mg and 250 mg, respectively. Participants spent more time preparing, and were willing to spend more time preparing the TRF than OxyContin®. In particle size analyses, the average number of particles < 850 μm was greater and the particle sizes were smaller for OxyContin®. Participants indicated they would pay "Less" (64%), or "The Same" (36%) for tablets that took more time and effort to prepare.

Study 2. The percent of subjects able to generate a solution was 92% for the 40 mg OxyContin® tablet, 36% for the 50 mg TRF, and 0% for the 250 mg TRF. OxyContin® solutions contained 37% oxycodone, whereas 50 mg TRF solutions contained 3.5% tapentadol. Participants spent longer preparing the 250 mg TRF than OxyContin®. There were no differences in amount of time participants would be willing to spend preparing the drugs for IV use. All participants indicated they would inject the OxyContin® solution, whereas 20% would inject the TRF 50 mg. Participants indicated they would pay "Less" (92%), or "The Same" (8%) for tablets that took more time and effort to prepare.

Conclusions: These data suggest that, when compared to a non-TRF, the tapentadol TRF reduced the ability of intranasal and intravenous users to successfully prepare this medication for abuse.

Financial Support: Johnson and Johnson Pharmaceuticals

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SMOKING CESSATION RCT BASED ON CBPR. DIFFICULT BUT FEASIBLE. AND BETTER.

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Aims: Smoking prevention and cessation interventions have proved effective among middle and high-income participants. But utilization and effectiveness of services are usually lower among poor and underserved populations, indicating a need for better alternatives. Randomized Clinical Trials (RCTs) are gold standard for testing interventions but render information that cannot speak to the needs of the poor and underserved, often excluded from these trials due to co-morbidities and mutual mistrust. A Community-Based Participatory Research approach (CBPR) might help develop rigorous research that directly addresses the needs of minority and low-income populations.

Methods: Data are from a CBPR-RCT aimed at comparing individual and a group cessation intervention arms. Participants were recruited and randomized from a low-income urban setting in mid Atlantic area. Participants in both arem received training on smoking cessation according to the Fresh Start curriculum on their 12 weekly sessions, receive pharmacotherapy and NRT upon their request and the clinician's medical evaluation. All participants were encouraged to attend the follow up cessations that lasted for nine months after the termination of the program.

Results: The trial is still under way and cessation data will be available by CPDD's conference. We focus here upon data collected at baseline through a self-administered questionnaire. The project recruited 275 participants to attend an orientation session, about 10 times more than prior to the CBPR project! Patients are mostly males (62%), 40 years of age or older (71%), African American (61%), with low education attainment (73% high school or less), unemployed (62%), with nicotine dependence (high=55%, moderate=39% according to the FNT).

Conclusions: Partnering with the community to design and implement RCT can be challenging and time consuming, but efforts are rewarded with opportunities to recruit participants often under-represented in trials.

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METHYLPHENIDATE INCREASES CIGARETTE SMOKING IN ADHD DIAGNOSED ADULTS.

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Aims: Stimulant medications increase cigarette smoking when administered acutely under controlled laboratory conditions to non-ADHD adults. Whether stimulants increase smoking behavior in ADHD diagnosed individuals is unknown. The aim of this experiment was to determine whether acute methylphenidate administration influences smoking behavior in ADHD diagnosed adults.

Methods: Nine participants that smoked 10-20 cigarettes per day, currently met diagnostic criteria for ADHD, were not currently prescribed ADHD medication and did not have other medical or psychiatric conditions (except nicotine dependence) completed the study. Participants completed 5, 6-hour experimental sessions. Doses of methylphenidate (10, 20 and 40 mg) were tested once while placebo was tested twice. One hour after medication administration, participants were allowed to smoke ad libitum for four hours. Measures of smoking included total cigarettes smoked, total puffs and carbon monoxide levels. Caloric intake during the four-hour smoking session was also calculated. Data were analyzed using planned comparisons between placebo and active doses. We hypothesized that methylphenidate would increase cigarette smoking and decrease caloric intake in ADHD diagnosed adults.

Results: Methylphenidate produced increases on a number of smoking measures (i.e., total cigarettes smoked, total puffs, exhaled carbon monoxide) and decreased caloric intake.

Conclusions: These results extend previous findings regarding the effects of methylphenidate on smoking to a clinically relevant population. Importantly, we observed increases in smoking measures at both therapeutic (i.e., 10 mg) and supratherapeutic (i.e., 40 mg) doses. The current findings have important clinical implications for the pharmacological management of ADHD in cigarette smokers or those that are at elevated risk to smoke.

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SEQUENCED VS. INTEGRATED TREATMENT FOR CO-OCCURRING DEPRESSION AND SUBSTANCE USE DISORDERS IN ADOLESCENTS.

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Aims: The primary aim of this study is to evaluate the optimal service delivery method for integrating empirically supported treatments (EST) for depressive disorders and non-nicotine substance use disorders (SUD) in an effort to improve treatment engagement, response, and maintenance of gains. Two ESTs, Adolescent Coping with Depression course (ACWD) and Functional Family Therapy (FFT), were implemented in sequence or in integrated fashion (IT). We hypothesized that IT would result in higher levels of engagement, attendance and retention.

Methods: 116 adolescents with depression and non-nicotine substance use disorders were recruited with their families and randomly assigned to one of three interventions: (a) ACWD followed by FFT (Sequence 1) (b) FFT followed by ACWD (Sequence 2), and (c) one combining and augmenting FFT and ACWD (Integrated Treatment; IT). Each arm consisted of 24 sessions provided over 20 weeks. Mean age of adolescents was 16.5, 74% were male and 50% non-Hispanic White. Assessment occurred at pretreatment, 10 and 20 weeks during treatment and 4 months later.

Results: Analyses were conducted in a 3x4 multivariate repeated measures ANOVA. All patients showed significant reductions in both depression and substance use.. Both IT and FFT-ACWD resulted in significant higher mean attendance rates than ACWD-FFT (8.5 vs 6). Similar results were found for engagement/retention with 54% of ACWD-FFT participants attending more than 6 sessions compared to 78% for FFT-ACWD and 83% for IT.

Conclusions: Taken together, these findings suggest that, integrated treatment is superior to either of the other sequences for attendance, engagement and retention. There appears to be a window of opportunity to engage adolescents in treatments for their depression and substance use and it may be especially difficult to engage families of youth if family-based treatment is not provided early in care.

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MATERNAL CANNABIS DEPENDENCE AND OFFSPRING EARLY SUBSTANCE INVOLVEMENT: RESULTS FROM AUSTRALIAN CHILDREN OF TWINS.

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Aims: We examined the impact of rearing by a cannabis dependent (CD) mother on offspring risk for early substance involvement.
Methods: Data from 478 adolescent offspring of 315 monozygotic (MZ) or dizygotic (DZ) twin mothers were drawn from ongoing studies of Australian children of twins. Cox proportional hazards regression was used to predict self-report age at first alcohol use, first alcohol intoxication, first cigarette use, onset of regular smoking, and first use of cannabis from dummy variables coding for high genetic and environmental risk (Group 1: mother CD+), high genetic but reduced environmental risk (Group 2: mother CD-, MZ cotwin CD+; Group 3: mother CD-, DZ cotwin CD+), and low genetic and environmental risk (Group 4: mother and cotwin CD-).
Results: Offspring from Groups 1 and 2, but not Group 3, demonstrated greater risk for early use of cigarettes, regular smoking and cannabis use, compared to control offspring (Group 4), with nonsignificant differences between Groups 1 and 2. Findings for first alcohol use and alcohol intoxication were inconclusive.
Conclusions: Results provide preliminary support for a genetic versus environmental pathway by which maternal cannabis dependence is associated with early and regular smoking and early cannabis use.
Financial Support: DA023696

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DECISION-MAKING AND IMPULSIVITY IN PTSD AND CO-OCCURRING COCAINE OR ALCOHOL DEPENDENCE: PRELIMINARY ANALYSES.

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Aims: To describe and compare measures of decision-making and impulsivity in 2 cohorts of subjects with PTSD and substance use disorders (SUDs). To explore the relationships between substance use, PTSD, and decision-making/impulsivity.
Methods: Preliminary data were drawn from 2 studies: the first examining risky behavior in women with cocaine dependence and PTSD (Women N=12), the second studying treatment of alcohol dependence in veterans with PTSD (Veterans N=12). Data included demographics, substance use measures, PTSD symptoms, impulsivity (Balloon Analog Risk Task [BART]) and decision-making (Delay Discounting [DD]).
Results: Women: mean age 43±10 yrs, 58% African American, all had cocaine dependence. Veterans: 83% male, mean age 53±11 yrs, 50% White, all had alcohol use disorders. Women mean days of cocaine use in the past 30 was 13±8, mean cocaine use was $145 ± $126 worth/week; Veterans mean days of alcohol use in the past 30 was 20±9, mean drinks/week was 39±18. Women mean CAPS score was 31±13 in subthreshold group and 84±22 in full PTSD group; Veterans mean CAPS score was 78±13 (all had full PTSD). CAPS scores did not differ by study group in those with full PTSD. Women and Veterans BART scores did not differ (with or without subthreshold PTSD cases). Their discounting of delayed rewards also did not differ. BART and DD scores did not correlate with frequency or quantity of substance use or with PTSD symptom severity in either group.
Conclusions: This preliminary analysis did not show differences in CAPS, BART, and DD scores in these two small cohorts of Women and Veterans with PTSD and co-occurring SUDs. In contrast to other studies, BART and DD did not appear to be related to substance use measures or PTSD symptoms. Objective measurement of impulsivity and decision-making in PTSD and co-occurring SUDs is in its early stages and analyses of larger samples are needed to clarify our findings.
Financial Support: Waldrop: NIH K23DA018718, Batki: DoD W81XWH-05-2-0094.
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SOCIODEMOGRAPHIC AND CLINICAL PREDICTORS OF TREATMENT RETENTION AND SUBSTANCE USE OUTCOMES.

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Aims: To identify for whom brief interventions for drug use are most effective, data from four NIDA Clinical Trials Network randomized clinical trials of Motivational Interviewing (MI) and Motivational Enhancement Therapy (MET) [CTN-0004 (Ball et al., 2007), CTN-0005 (Carroll et al., 2006), CTN-0013 (Winhusen et al., 2008), and CTN-0021 (Carroll et al., 2009)] were combined for secondary data analysis.
Methods: Participants (N=1390, 37% White, 36% female) were recruited from treatment programs across the nation. CTN-0013 recruited pregnant substance users; CTN-0021 recruited Spanish-speaking participants. All other inclusion/exclusion criteria were similar. Participants were randomized to Treatment as Usual (TAU) or MI (1 session, CTN-0005)/MET (3 sessions). Baseline data were analyzed using logistic regression to identify predictors of treatment completion and drug use 4 weeks post-randomization.
Results: For the combined MI/MET group, higher baseline Addiction Severity Index (ASI) Alcohol and Medical scores are associated with higher odds of treatment completion (OR=1.11 and 1.09, respectively) while higher ASI Drug Use scores are associated with lower odds of completion (OR=0.79). Whites, Blacks, and Hispanics all had lower odds of completion compared with "other" race (OR=0.32, 0.23, and 0.19, respectively). Higher scores on ASI Drug Use (OR=0.62) and Medical (OR=0.91) subscales and any baseline drug use (OR = 0.17) were associated with lower odds of abstaining from drugs at week 4; similar results were found for TAU. In addition, for Hispanics in the MI/MET group, there was a significant interaction such that a higher ASI Family score is associated with higher odds of abstaining (Wald Chi-square=8.7, p=.0032, OR=1.51).
Conclusions: Preliminary analyses indicate race and baseline alcohol, medical, and drug use status predict treatment completion and drug abstinence status post-treatment for MI/MET participants. These predictors may be helpful in identifying who may be best suited for brief substance use interventions.
Financial Support: NIDA Clinical Trials Network grant #U10 DA020024

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RISK FACTORS FOR NON-FATAL OVERDOSE AMONG HIV-INFECTED RUSSIANS WITH HEAVY ALCOHOL USE.

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Aims: Fatal and non-fatal overdoses are common among Russian heroin users, yet risk factors among HIV-infected Russians have not been studied. We examined overdose and its potential risk factors in a cohort of HIV-infected Russians with heavy alcohol use.
Methods: We analyzed baseline data of 401 participants in the HERMITAGE Study, an HIV secondary prevention trial for persons reporting "heavy" alcohol use (NIAAA risky drinking definition) and risky sex in the past 6 months. Outcomes were any lifetime overdose (substance not specified) and any overdose in the last 3 months. We examined age, CD4 cell count, depressive symptoms (measured via the Beck Depression Index II), any lifetime suicidal thoughts or attempts, any lifetime heroin use (for any lifetime overdose), 30 day heroin use (for any 3-month overdose), and 12-month alcohol dependence (via the CIDI-short form). Factors associated with overdose were identified using stepwise multivariable logistic regression models.
Results: Participants' characteristics included median age 29 years, 42% female, and median CD4 cell count 326. Over two-thirds (69%) reported a lifetime history of overdose; 11% reported overdose in the past 3 months. Risk factors associated with lifetime overdose in multivariable models were lifetime suicide attempts or thoughts (adjusted odds ratio [AOR] 2.20 95%CI: 1.33-3.66), lifetime heroin use (AOR 7.66 95%CI: 4.31-13.61), and alcohol dependence (AOR 1.69 95%CI: 1.02-2.81). The only significant risk factor for past 3-month overdose was past 30-day heroin use (AOR 3.29 95%CI: 1.26-8.60).
Conclusions: Nonfatal overdose among HIV-infected Russians with heavy alcohol use is common. Risk factors, similar to those seen in other populations, include heroin use, suicidal thoughts or attempts, and alcohol dependence. Overdose prevention efforts are needed among HIV-infected Russians with heavy alcohol use.
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EFFECTS OF THE NK-1 ANTAGONIST, APREPITANT, ON RESPONSE TO OXYCODONE IN HUMANS.

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Aims: Recent evidence suggests that inactivation of substance P receptors (NK1), either through genetic deletion or pharmacological blockade, significantly attenuates the rewarding effects of opioids in an array of laboratory models. Here we tested the hypothesis that pretreatment with the NK-1 antagonist, aprepitant (Emend®), reduces the direct pharmacodynamic actions of oxycodone related to its rewarding effects in humans.
Methods: Healthy adult inpatient volunteers with prescription opioid abuse participated in a total of 15 experimental sessions. The effects of 2-hr pretreatment with aprepitant (0, 40 or 200 mg, p.o.) on response to placebo or oxycodone (15 & 30 mg, intranasal; 20 & 40 mg, p.o.) were examined under randomized and double-dummy conditions. An array of physiological, subject- and observer-rated, and performance measures was collected for 30 min before and at regular intervals for 5 hr after oxycodone administration.
Results: Oxycodone produced orderly and dose-related increases on prototypic mu opioid agonist effects, including miosis, respiratory depression, and increased subject ratings of "liking" and "good effects" by both routes of administration. There were significant route differences for the time required to reach peak effects, with maximal responses occurring earlier for intranasal compared to oral oxycodone ($p<.05$). There was no evidence that aprepitant reduced the effects of oxycodone on any measures, and the highest dose of aprepitant produced modest, but nonsignificant, increases of subjective ratings ("liking" and street value) and miosis after oxycodone.
Conclusions: These data do not support the hypothesis that acute pretreatment with an NK-1 antagonist reduces the pharmacodynamic effects of mu opioid agonists related to their rewarding properties.
Financial Support: This work was funded by NIDA R01 DA027031 (SLW), Merck Sharp & Dohme Corp., a subsidiary of Merck & Co, Inc. (drug supply) and the UK CR-DOC (inpatient support).

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DETERMINANTS OF HEALTH-RELATED QUALITY OF LIFE AMONG METHADONE MAINTENANCE SUBJECTS IN TAIWAN.

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Aims: To compare health-related quality of life (HRQOL) of methadone maintenance treatment (MMT) patients with healthy controls and to explore the determinants of HRQOL in the MMT patients.
Methods: In this cross-sectional study, WHOQOL-BREF was administered in heroin-dependent subjects stabilized on MMT for at least 3 months. Demographics and factors related to methadone treatment were obtained from clinical interview and medical records. The HRQOL in this sample was compared to that of an age-, sex-, education- and municipality– matched reference population taken from a national survey in Taiwan. The determinants of HRQOL were analyzed by analysis of covariance (ANCOVA) method.
Results: The mean age of the 373 subjects was 37.8±7.8 years and 80% was male. The current methadone daily dose was 54.7±28.1 mg/day and the average treatment duration was 64 weeks. All of the four domains' scores of WHOQOL-BREF, i.e. physical, psychological, social and environmental, were significantly lower in the MMT subjects than in the healthy controls (all $p<0.005$). In analysis of the determinants of HRQOL in MMT patients, male(β=-4.29, $p<0.01$),unemployment(β=-7.13, $p<0.0001$),use of alcohol in the last 4 weeks(β=-0.14, $p<0.05$),previous MMT experience(β=-4.69, $p<0.0001$)and adverse events related to methadone(β=-0.38, $p<0.0001$) were significantly associated with poor HRQOL.
Conclusions: These findings highlight the importance of holistic approach to improve outcomes of various dimensions among the methadone maintenance subjects.
Financial Support: This study is supported by National Health Research Institutes, Taiwan.

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THE GLT-1 ACTIVATOR CEFTRIAXONE ATTENUATES BEHAVIORAL AND NEUROCHEMICAL EFFECTS OF COCAINE IN RODENTS.

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Aims: No medication is approved to treat cocaine addiction, but mounting evidence suggests glutamate-directed approaches may reduce cocaine dependence and relapse. One of the most promising but least understood glutamate targets is glutamate transporter subtype 1 (GLT-1), a predominantly astrocytic transporter that mediates about 90% of total forebrain glutamate uptake. In the present set of experiments, we assessed effects of the GLT-1 activator, β-lactam antibiotic ceftriaxone (CTX) against cocaine in several behavioral assays.
Methods: We tested the hypotheses that repeated CTX administration (200 mg/kg) would disrupt cocaine locomotor sensitization, self-administration (SA), and conditioned place preference (CPP) in rodents, and that such treatment would also reduce basal and cocaine-sensitized extracellular glutamate in the nucleus accumbens.
Results: Results showed that repeated CTX attenuates cocaine-induced locomotor sensitization and reduces cocaine (0.56 mg/kg/inf) but not sweet food (50% Ensure) SA under fixed ratio 1 and progressive ratio schedules. However, CTX does not prevent the development of cocaine (10, 20 mg/kg) CPP. Results also showed that CTX treatment reduces basal accumbens core glutamate, an effect that is blocked by a GLT-1 inhibitor, and that CTX attenuates cocaine-sensitized accumbens glutamate levels as well.
Conclusions: These results suggest that the GLT-1 activator CTX selectively reduces the reinforcing strength of cocaine, potentially via suppression of cocaine-induced changes in glutamate signaling within the nucleus accumbens core.
Financial Support: This work was supported by National Institutes on Drug Abuse RC1 DA028153 (SMR)

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TRAUMA EXPOSURE, PTSD, AND SUBSTANCE ABUSE: A CASE CONTROL STUDY OF WOMEN IN PRISON AND IN THE GENERAL POPULATION.

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Aims: To compare the prevalence of childhood and adult abuse/trauma exposure and PTSD, and their relationship with substance abuse problems, among incarcerated women and women in the general population.
Methods: 100 incarcerated women (participants in a prison substance abuse treatment program) were matched on socio-demographics with 100 women in the general population using the NESARC sample. A case-control method was used to examine the comparative odds of abuse/trauma exposure and the relationship of abuse/trauma exposure with PTSD using logistic regression.
Results: Incarcerated women had significantly higher odds of several types of abuse/trauma exposure than matched controls in the general population, including serious accident, illness, or disaster (OR=2.1, 95% CI = 1.5,2.9); physical or sexual trauma (OR=3.7, CI=2.4, 5.7); sudden death of family member or friend (OR=1.7, CI= 1.3,2.4); childhood neglect (OR=1.7, CI=1.3,2.2); childhood physical or emotional abuse (OR=1.9, CI=1.4,2.6); witness family violence as child (OR=1.9, CI=1.5,2.4); and childhood sexual abuse (OR=1.9, CI=1.5,2.4). Lifetime prevalence of PTSD was higher among incarcerated women (40% vs. 12%, $p < .001$) and they were also more likely to report having used drugs in response to traumatic events (64% vs. 6%, $p < .001$). A multivariate logistic regression model found that exposure to intimate partner violence increased the odds of PTSD (OR=4.5, CI=1.4, 14.7, $p < .02$), as did using alcohol or drugs in response to trauma (OR=8.8, CI=2.5, 30.7, $p<.0001$). Having an incarcerated parent about doubled the odds of PTSD ($p <.02$), although this effect was marginally stronger among women in the general population than incarcerated women.
Conclusions: Childhood and adult abuse/trauma exposure is significantly more prevalent among incarcerated women than among comparable women in the general population. PTSD was uniquely associated with intimate partner violence and substance abuse in both samples, suggesting an underlying common dynamic.
Financial Support: Supported by the California Department of Corrections and Rehabilitation (contract no. C08.106)

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DELAY DISCOUNTING AS A PREDICTOR OF TREATMENT RESPONSE AMONG COCAINE-DEPENDENT OUTPATIENTS.

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Aims: Delay discounting (DD) describes the rate at which reinforcers lose value as the temporal delay to their receipt increases. Greater discounting has been associated with vulnerability to substance use disorders, including cocaine use disorders. The present study examined whether DD of hypothetical monetary reinforcers predicts the amount of cocaine abstinence achieved among cocaine-dependent adults enrolled in outpatients treatment.
Methods: Participants were 36 adults who were participating in a randomized controlled trial examining the efficacy of voucher-based contingency management (CM) using low-magnitude (N = 18) or high-magnitude (N = 18) voucher monetary values.
Results: DD predicted the number of continuous weeks of cocaine abstinence achieved, after adjusting for treatment condition during the initial 3-month ($t(33) = 2.48$, $p < .05$) and 6-month periods ($t(33) = 2.40$, $p = .02$). Greater discounters achieved less abstinence in the Low-magnitude voucher condition (3-month: $t(16) = 2.48$, $p = .03$; 6-month: $t(16) = 2.68$, $p = .02$), but not in the High-magnitude voucher condition (3-month: $t(16) = 0.51$, $p = .62$; 6-month: $t(16) = 1.08$, $p = .30$), although the interaction between DD and treatment condition was not significant (3-month: $t(32) = -1.12$, $p = .27$; 6-month: $t(32) = -0.37$, $p = .71$).
Conclusions: These results provide further evidence that DD can predict treatment outcomes in a new clinical population (i.e., cocaine-dependent outpatients) while also suggesting that a more intensive intervention like the High-magnitude CM condition may diminish the negative relationship between DD and treatment response.
Financial Support: This research was supported by research grant R01DA009378 and training grant T32 DA07242 from the National Institute on Drug Abuse.

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HUMAN MDMA (ECSTASY) USERS HAVE ALTERED BRAIN ACTIVATION DURING SEMANTIC ENCODING.

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Aims: MDMA (Ecstasy) is neurotoxic to serotonin axons and MDMA users have impaired verbal memory. Recent studies have correlated long-term MDMA use with reduced gray matter and altered functional brain activation in regions that play a role in verbal memory. The aim of our study was to examine the long-term neurophysiological effects of MDMA use on semantic processing.
Methods: 34 right-handed subjects (11 Controls [age 22.36 years], 23 abstinent MDMA Users [age 24.57 years] performed a semantic encoding task during functional MRI acquisition. Subjects were told to memorize (encode) 20 words and 20 pseudo-words (pronounceable non-words) that were presented using a randomized rapid event-related design. To isolate brain regions activated during semantic encoding, we created statistical activation maps in which brain activation was greater for word encoding than for pseudo-word encoding (cortical mask; corrected $p = .01$; cluster size = 276 voxels).
Results: MDMA users had greater activation than controls in two large clusters with peak activations in the right superior parietal lobule and left precuneus. An analysis of sub-regions included in the larger clusters revealed that MDMA users had greater activation during semantic encoding bilaterally in language processing regions, including the precuneus, inferior parietal lobule, and Brodmann area 40 as well as in the right angular gyrus.
Conclusions: These findings demonstrate that MDMA users have increased brain activation during semantic processing. This increase in brain activation suggests that MDMA users have reduced cortical efficiency during semantic encoding, possibly secondary to MDMA-induced serotonin neurotoxicity. These preliminary findings provide additional support for altered cerebral neurophysiology as a consequence of MDMA exposure in humans.
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WILLINGNESS TO QUIT SMOKING AMONG SUBSTANCE ABUSE RECOVERING PATIENTS.

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Aims: The aim of this research was to examine the predictors of willingness to quit smoking cigarettes among patients who were recovering from alcohol and other illicit drug abuse dependence.
Methods: Twelve hundred thirty-six patients who were recovering from alcohol and other illicit drug abuse dependence in a mid-Southern state in the United States were interviewed about their smoking status and willingness to quit smoking within 30 days and 6 months at the time of 6 month follow-up.
Results: Of these patients, 76.9% (n = 950) reported being a current smoker. Close to 16% (n = 148) of the current smokers expressed an interest in quitting smoking within 30 days and about 35% (n = 327) within six months at the time of the 6-month follow-up interview. Logistic regression analyses revealed a few significant correlates of willingness to quit smoking: lower Fagerstrom nicotine dependence levels and being African American correlated with willingness to quit within 30 days and 6 months at the time of the 6-month follow-up interview. Not using marijuana/hashish or opiates at intake and being female were only correlated with willingness to quit within 30 days at the time of follow-up.
Conclusions: The results of this study could be utilized in identifying substance abuse clients more likely to participate in smoking cessation intervention programs, if such programs were offered by treatment
facilities.
Financial Support: This research was sponsored by the University of Memphis.

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PROFILE OF GLUTAMATE ANOMALIES OBSERVED WITHIN THE ACCUMBENS CORE DURING SHORT-TERM WITHDRAWAL FROM EXCESSIVE COCAINE INTAKE.

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Aims: The influence of moderate-dose cocaine regimens upon indices of glutamate transmission within the nucleus accumbens (NAC) has been relatively well-characterized. However, considerably less is known regarding the consequences of excessive cocaine intake upon extracellular glutamate levels or the expression and functional status of glutamate receptors within the NAC core subregion.
Methods: Groups of rats were trained to lever-press for 0.25 mg/infusion of cocaine during 10 daily 6-hr sessions. Control animals received daily 1-hr training to lever-press for saline. At 3 days following the last self-administration session, the NAC core was processed by immunoblotting for various glutamate-associated proteins. Other rats were subjected to no net-flux and reverse dialysis procedures to examine for effects of excessive cocaine intake upon basal NAC core glutamate content and for Group1 metabotropic glutamate receptor function.
Results: Compared to saline controls, cocaine self-administering animals exhibited: (1) lowered levels of Homer1b/c but higher levels of mGluR1, phospho-ERK and phospho-PKC epsilon at 3 days withdrawal; (2) reduced basal extracellular glutamate content, but no change in glutamate clearance; and (3) a non-significant increase in Group1 mGluR-stimulated glutamate release.
Conclusions: Short-term withdrawal from excessive cocaine intake produces certain anomalies in NAC core glutamate transmission that are consistent with those reported following more moderate cocaine regimens, including reduced basal glutamate content and reduced Homer1b/c expression. However, in contrast to other models, excessive cocaine self-administration elevated, rather than lowered, mGluR1 expression and function in the NAC core. These data indicate that a history of excessive cocaine intake produces a unique profile of glutamate anomalies, the functional relevance of which are deserving of further investigation.
Financial Support: NIDA grant DA024038 to KKS, DA and UCSB Academic Senate to OBS and KKS.

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MITIGATION OF MORPHINE-INDUCED RESPIRATORY DEPRESSION WHEN MORPHINE SULFATE AND NALTREXONE HYDROCHLORIDE EXTENDED RELEASE CAPSULES ARE CRUSHED AND INJECTED.

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Aims: Respiratory depression (RD) is the leading cause of death following misuse/abuse of opioid drugs. When morphine is abused intravenously (IV), RD may occur within minutes and may become fatal within 3h of overdose; however, it may be reversed by timely administration of an opioid antagonist. Unfortunately, timely intervention is not always available. Morphine sulfate and naltrexone hydrochloride extended release capsules (MS-sNT; EMBEDA®) contain pellets of extended-release morphine with a sequestered naltrexone core; when tampered with the pellets release both morphine and naltrexone. When morphine and naltrexone were administered IV in the 25:1 ratio found in MS-sNT, naltrexone abated morphine-induced euphoric effects. Hypothesis: In this study, following IV administration of morphine and naltrexone (25:1 ratio), morphine-induced RD will be reduced vs. that of IV morphine alone.
Methods: Exploratory analyses of end-tidal CO2 (EtCO2) were performed during a single-dose, 3-way crossover study comparing pharmacodynamic (PD) effects (drug liking, euphoria) of morphine sulfate 30mg administered IV with naltrexone HCl 1.2mg vs. IV morphine sulfate 30mg administered alone or normal saline (placebo) in 28 opioid-experienced, non-opioid-dependent men.
Results: Significant differences were detected in LS means between active treatment groups for Emax and partial AUEs ($p<0.01$). No difference was detected between the combination morphine+naltrexone and placebo groups in EtCO2 levels ($p=0.3064$), which emphasized naltrexone's PD effect of morphine displacement on the μ-opioid receptor.
Conclusions: Results suggest that abuse of the MS-sNT formulation by extraction and injection could mitigate the risk of potentially fatal morphine-induced RD. The uniqueness of this finding is that the harm reduction potential is already built into the medicine.
Financial Support: King Pharmaceuticals®, Inc.

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WORK HISTORIES AND EMPLOYMENT NEEDS OF DRUG COURT CLIENTS.

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Aims: Employment has been identified as an important drug abuse treatment outcome and is associated with a decrease in the likelihood and severity of relapse, criminal activity, and related problems. Yet, drug abusers, particular those with criminal histories, face a variety of barriers in obtaining employment. The present has the following aims: 1) Describe the work experience in a sample of drug court clients; 2) Assess the perceived employment barriers and needs of this group; and 3) Identify future employment goals.
Methods: As part of a randomized trial of an employment intervention, baseline data were collected from 50 unemployed drug court participants during face-to-face interviews. Information about their work histories and employment barrriers/needs was obtained. Participants also completed the Barriers to Employment Success Inventory (BESI) and the Occupational Work Ethic Inventory (OWEI).
Results: Most participants' recent work history included jobs as a service worker (42%), an operative (20%), or other laborer (16%, but 60% anticipated having a professional position within 5 years. In past 12 months, participants were paid an average of 83.5 days for legal work and 139.7 days for illegal work. Childcare (56%), transportation (36%), and overcoming the stigma of their criminal record (26%) were the most often reported barriers. BESI scores suggest that job-seeking knowledge and career planning skills (M=2.2) are additional barriers. OWEI scores (M=5.9) suggest that this group has a good work ethic.
Conclusions: These findings suggest that employment interventions should be tailored for drug-involved offenders, including strategies for effectively minimizing the impact their criminal history has on obtaining employment. Despite these barriers, participants were motivated, reported good work ethics, and maintained a positive outlook out their employment futures. Educating employers about these positives may help in reducing the stigma that drug-involved offenders face.
Financial Support: This research is supported by NIDA grant R21DA021178.

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A BRAIN IMAGING STUDY INTO NICOTINE-INDUCED DOPAMINE RELEASE IN CIGARETTE SMOKERS IN TREATMENT WITH BUPROPION USING [11 C] RACLOPRIDE IN POSITRON EMISSION TOMOGRAPHY.

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Aims: Although imaging studies show that release of DA follows smoking, little is known regarding how common genetic polymorphisms for three genes associated with smoking (dopamine D2 receptor, dopamine and serotonin transporter) interact with smoking status and modulate individual differences in nicotine-induced DA release. The specific aim of this experiment is to examine whether dopamine release in the striatum as a result of smoking cigarettes containing nicotine in regular cigarette smokers can predict outcome of smoking cessation treatment with bupropion. Secondly, to examine whether genetic variations of the dopamine receptor and transporter contribute to dopamine release in these individuals during treatment.
Methods: 10 participants were treated with Bypropion (Zyban) for 2 months and weekly sessions of personal counseling. They were scanned at week 7 with bolus and constant infusion of [11C] Raclopride in PET before and after smoking a nicotine cigarette.
Results: Preliminary results in 7 subjects showed that the males (n=3) have released more dopamine in the caudate (14.53%) and in the putamen (15.73%) than females (n=4) in caudate (2%) and putamen (1.68%) respectively. Secondly, there was negative correlation of the reported number of cigarettes smoked before treatment and the % of nicotine-induced dopamine released in the caudate ($r=-0.66$ $p<0.05$).
Conclusions: Heavy smokers tend to release less dopamine while smoking a cigarette during treatment. It is plausible that they need to smoke more cigarettes in order to release dopamine and experience associated pleasure from smoking. This may constitute a vulnerability factor during the treatment phase of smoking cessation and maintenance against relapse.
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PREDICTORS OF OUTCOME IN THE MULTI-SITE CTN PRESCRIPTION OPIOID ADDICTION TREATMENT STUDY.

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Aims: The 10-site Prescription Opioid Addiction Treatment Study, conducted as part of the NIDA Clinical Trials Network, examined different lengths of buprenorphine-naloxone (bup-nx) treatment with different intensities of counseling for patients dependent upon prescription opioids. The aim of the current study is to examine predictors of treatment outcome in this patient population.
Methods: A 2-phase adaptive treatment research design examined outcomes 1) during a brief taper and 2) while maintained on bup-nx for 12 weeks. "Successful outcome" was defined as abstinence in week 12 of Phase 2 (the last week of bup-nx stabilization) and ≥2 of the previous 3 weeks (weeks 9-11). Sociodemographic and clinical characteristics were examined as predictors of successful outcome.
Results: Bivariate analyses revealed several predictors of successful outcome. Those who had never used heroin were more likely to achieve successful outcomes than those who had ever used heroin (54% vs. 37%, $p<.01$). Those reporting sustained-release oxycodone as the primary opioid used in the 30 days before baseline had fewer successful outcomes (41%) than did those who primarily used other opioids (58%, $p<.001$). Those who had never attended self-help meetings had more successful outcomes than those who had ever done so (52% vs. 38%, $p<.05$). Other predictors of successful outcome included major depressive disorder in the past year (64% of those with the diagnosis vs. 46% of those without, $p<.01$), and being older (mean of 33.9 years vs. 31.2 years, $p<.01$). The presence of chronic pain at baseline did not predict outcome.
Conclusions: Among patients with prescription opioid dependence, characteristics traditionally associated with addiction (use of heroin, absence of psychiatric illness, attendance at self-help meetings) were associated with poorer outcomes. Further examination of these variables may help to understand the interrelationships among them.
Financial Support: NIDA grants U10DA015831, K24DA022288, U10DA020024, K23DA022297, and U10DA013045

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PREDICTORS OF SEVERE PRESCRIPTION DRUG ABUSE AMONG COLLEGE STUDENTS USING THE RADARS® SYSTEM COLLEGE SURVEY.

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Aims: The prevalence of non-medical prescription drug use (NMDU) among US college students is increasing. This analysis aimed to characterize demographic and behavioral predictors of severe drug abuse problems among college students reporting NMDU.
Methods: Data from RADARS System College Survey, a nationally representative web-based survey of NMDU in college students, were used (3Q2010). Respondents endorsing use of one or more prescription medications (opioids, stimulants, muscle relaxants, anxiolytics, anti-depressants, or sleep-aids) in the past 3 months for any reason other than what was prescribed by their doctor were included (n=569). All respondents completed a validated drug abuse screening instrument, the DAST-10. Low DAST-10 was defined as scoring ≥ 5, and High DAST-10 was defined as scoring ≤ 6. Chi-squared tests and t-tests were used to compare demographic and behavioral characteristics of respondents with High vs. Low DAST-10 scores.
Results: The High DAST-10 group was more likely male (50% vs. 30%, p<.001), Hispanic ethnicity (36% vs.15%, p<.001), a fraternity/sorority member (48% vs.20%, p<.001), and a tobacco user (75% vs.53%, p<.001). The high DAST-10 group was more likely to report NMDU of more than one prescription drug class (p<.001). The High DAST-10 group was more likely to have used illicit drugs in the past 3 months (marijuana, MDMA, cocaine, crystal meth, hallucinogens, and heroin, p<.001). The High DAST-10 group was more likely to report reasons for their NMDU; "to get high" (20% vs.13%, p<.05), "curiosity" (18% vs.7%, p<.001), or "to treat withdrawal symptoms" (6% vs. 2%, p<.05).
Conclusions: College Students with severe problems related to drug abuse may be abusing several prescription drug classes as well as illicit drugs; this should be considered when designing interventions for this population.
Financial Support: The RADARS System is a public non-profit organization providing post-marketing surveillance of prescription medications to pharmaceutical manufacturers.

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APPLYING WEB-BASED TECHNOLOGY TO DISSEMINATE MOTIVATIONAL INTERVIEWING: A USABILITY STUDY.

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Aims: Examine the overall access and usability of a website designed to be a resource for disseminating motivational interviewing (MI) materials and information.
Methods: Since 1999, the Mid-Atlantic Addiction Technology Transfer Center (Mid-Atlantic ATTC) has maintained a website (www.motivationalinterview.org) for the purpose of providing (1) a bibliography of MI-specific scientific literature, (2) MI training materials, (3) a list of the Motivational Interviewing Network of Trainers, and (4) a schedule of MI training events. Although a cursory look at the website analytics shows that the site generates a great deal of traffic, little was known about the actual impact and effectiveness of the site in meeting the needs of substance abuse treatment professionals interested in obtaining MI resources. Therefore, a complete analysis of the website statistics was conducted that included search parameters used to locate the site, number of hits, length of site visits, and the most frequently accessed information.
Results: Examination of the website analytics revealed a daily average of 1,811 (approximately 54,500/month) visits to the MI website, with more than half (55%) of those visits lasting less than 30 seconds. The majority of the visits were the result of individuals conducting a Google search and the most frequently visited pages were those that provide a definition of MI, resource downloads, and how to locate a trainer or training (complete system-level data will be provided).
Conclusions: Although the site generates a great deal of traffic, the analytics suggested that site navigation needed to be improved to fully meet the needs of practitioners interested in obtaining MI-specific resources. Based on these findings, the site is being redesigned and analytics for the new site will be examined to assess the impact of the new design on the usability of the MI website.
Financial Support: Funded by the Mid-Atlantic ATTC SAMHSA/CSAT grant # 5UD1TI013415-09

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SHORTER INTERPUFF INTERVAL ASSOCIATED WITH GREATER NICOTINE INTAKE IN SMOKERS WITH AND WITHOUT SCHIZOPHRENIA.

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Aims: Understanding cigarette puffing parameters that determine nicotine intake may be essential to improving cessation outcomes for smokers with schizophrenia.
Methods: METHODS: One hundred sixty one smokers (75 schizophrenia; SCZ and 86 controls; CON) were assessed in a single day (24 + 2 h), ad libitum smoking topography session using the CReSSmicro device. The following variables were measured: time to first puff, number of cigarettes smoked, puffs per cigarette, puff volume, puff duration, inter-puff interval (IPI), peak flow, average flow and time to peak flow. Subjects also had 3 blood draws for nicotine and its metabolites on the same day.
Results: Smokers were not different in baseline characteristics including cigarettes per day, or total FTND score. Using mixed model analysis, smokers with SCZ were different on puffing variables including more puffs per cigarette, shorter IPI, shorter time to first puff and time to peak and greater total cigarette puff volume (all p<0.05). The mean/ median IPI was 16.0/9.4 sec in SCZ and 22.6/16.3 in CON, respectively. Serum nicotine and cotinine levels (drawn at 10am) were higher in SCZ vs. CON (Nic 22.0 vs. 16.3 ng/ml; p<0.01). A regression analysis determined that decreases in IPI were associated with increases in nicotine intake in SCZ and CON smokers (p<0.05).
Conclusions: This research confirms and builds upon prior findings of altered cigarette puffing in SCZ. Higher nicotine intake from smoking may be associated with shorter time between puffs.
Financial Support: This work was supported by a grant from the National Institute of Mental Health (R01-MH076672-01A1 to JMW).

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THE EFFECT OF TRADITIONAL MASCULINITY IN RESPONSE TO AN HIV RISK REDUCTION INTERVENTION FOR SUBSTANCE-ABUSING MEN.

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Aims: African Americans constitute over 50% of new HIV cases. Adherence to traditional notions of masculinity (TNM), coupled with substance abuse, can conflict with safe-sex practices (Noar & Morokoff, 2002). Thus, the aim of this study is to evaluate the effect of TNM on the relationship between treatment type and risky sexual behaviors. It is hypothesized that(1) African-American men who adhere less to TNM will reduce sexual risk behaviors more than men with allegiance to role norms; (2) the relationship between treatment type and risky sexual behaviors will be weaker for men as adherence to TNM increases.
Methods: This study will use data from the National Institute of Drug Abuse Clinial Trials Network (NIDA CTN0018)clinical evaluation of Real Men are Safe (REMAS), a male HIV intervention program demonstrated to reduce risky sexual behaviors among substance using men (Calsyn et al., 2009). The initial study recruited 116 African American men in outpatient drug treatment from 14 CTN sites across the nation. Following baseline assessments, all participants were randomized to either the 5-session REMAS intervention or an HIV education class. The Sexual Behavior Inventory collected at baseline and at 6-month follow-up was used to measure risky sexual behaviors. The BEM Sex Role Inventory Short-form was also administered and measured adherence to TNM before and after treatment. An expert panel will identify items on the BEM Sex Role Inventory Short Form that best reflect African-American male traditional notions about masculinity.
Results: 50% of White participants in REMAS significantly increased condom use compared to 35% of Whites in the control. However, 16% of Black men in REMAS were less likely to report condom use than Black men in the control condition (40%). Hierarchical linear regression modeling will be used to test group differences and sex role attitudes as a moderator. The number of unprotected sexual occasions will serve as the outcome measure.
Conclusions: These findings suggest that the efficacy of REMAS varies by ethnicity. Cultural factors must be examined.
Financial Support: Grant #: RC1D8028245-02.

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IDENTIFICATION OF A NOVEL ALLOSTERIC MODULATOR OF OPIOID RECEPTORS: SORI-25825.

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Aims: As part of an on-going project to identify novel non-peptide small-molecule mu agonist/delta antagonist compounds, we identified a compound, SoRI-25825, which partially inhibited [3H]DAMGO binding to mu opioid receptors. As this might indicate a non-classical "allosteric" effect, the purpose of this study was to characterize in vitro the interaction of this compound with the cloned mu, delta and kappa receptors.
Methods: Ligand binding studies followed published procedures and used CHO cells that stably express the cloned human mu, delta and kappa opioid receptors. [35S]-GTP-gamma-S functional ("GTP") binding assays followed published procedures, and used the NG108-15 neuroblastoma x glioma cell line for the delta receptor assay.
Results: SoRI-25825 partially inhibited mu binding (EC50=2170±380 nM, Emax=58±2%), delta binding (EC50=466±92 nM, Emax=81±3 nM) and kappa binding (EC50=322 nM, Emax=78±2%). In the "GTP" assay, SoRI-25825 (2.5, 5, 10, 20 μM) shifted the DAMGO-dose response to the right without changing the Emax value. However, the EC50 values did not shift to the right as far as expected, resulting in Ke values that increased in a dose-dependent manner. Similar findings were observed for delta "GTP" assay using SNC-80 dose-response curves. In the kappa "GTP" assay, SoRI-25825 (0.2, 1, 2.5 5 μM) shifted the (-)-U50,488-dose-response curve to the right and decreased the Emax in a dose-dependent manner. Kinetic dissociation experiments are currently in progress.
Conclusions: Taken together, our results indicate that SoRI-25825 interacts with opioid receptors in a non-classical "allosteric" manner.
Financial Support: Supported by the IRP, NIDA, NIH, DHH

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TREATMENT COMPLETION IN OPIOID-DEPENDENT PREGNANT PATIENTS RANDOMIZED TO AGONIST TREATMENT: THE ROLE OF INTRAVENOUS DRUG USE.

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Aims: To examine the relationship of intravenous drug use to treatment completion in opioid-dependent pregnant patients randomized to methadone *v.* buprenorphine treatment.
Methods: Participants were 175 opioid-dependent pregnant patients enrolled in the MOTHER study, a multi-site randomized controlled, double-blind, double-dummy trial comparing buprenorphine to methadone treatment, for which no difference in treatment completion was found between the two medication conditions.
Results: Of the 175 participants in this secondary data analysis, 1 was excluded due to missing data on key variables. Of the 174 remaining participants, 89 had been randomized to the methadone condition, and 85 to the buprenorphine condition. Of the 73 methadone participants who completed treatment, 28 were intravenous drug users (IDUs) and 45 non-intravenous drug users (NIDUs); of the 16 participants who did not complete, 6 were IDUs and 10 NIDUs. Of the 58 buprenorphine participants who completed treatment, 19 were IDUs and 39 NIDUs; of the 27 participants who did not complete, 12 were IDUs and 15 NIDUs. A logistic regression of IDU/NIDU, medication condition, and their interaction found no significant difference in treatment completion between IDUs and NIDUs randomized to methadone or buprenorphine.
Conclusions: These results suggest that IDU/NIDU status played no significant role in treatment completion in opioid-dependent pregnant patients randomized to either medication condition. Further research is needed to elucidate the relationship between intravenous drug use and other treatment outcomes for opioid-dependent pregnant patients on methadone *v.* buprenorphine to help guide clinical decision-making in this important population.
Financial Support: Funded through NIDA R01DA 045778, 015832, 015764, 015738, 017513, 018410, and 018417.

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THE RELATIVE RISKS OF OSMOTIC-RELEASE METHYLPHENIDATE TREATMENT FOR ADOLESCENT SUBSTANCE ABUSERS.

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Aims: Psychostimulants are effective treatments for attention deficit hyperactivity disorder (ADHD) but may be associated with abuse liability, misuse/diversion, and adverse effects. These risks are perceived to be greater in substance abusing adolescents relative to non-substance abusing adults. The present analysis evaluated the abuse liability, misuse/diversion, and adverse effects associated with the use of osmotic-release oral system methylphenidate (OROS-MPH), relative to placebo, for treating ADHD in adolescents with a substance use disorder (SUD) as a function of severity of use and compared these risks to those associated with the treatment of adults without a non-nicotine SUD.
Methods: Datasets from two randomized placebo-controlled trials of OROS-MPH for treating ADHD, one conducted with 303 adolescents (13-18) with at least one non-nicotine SUD and one with 255 adult smokers (18-55) were analyzed. Outcome measures included the Massachusetts General Hospital (MGH) Liking Scale, self-reported medication compliance, pill counts, and adverse events.
Results: Abuse liability and misuse/diversion of OROS-MPH was not significantly associated with substance use severity and did not differ significantly between the adolescent and adult samples. The adolescents lost more pills relative to the adults regardless of treatment condition, which suggests the importance of careful medication monitoring. Higher baseline use of alcohol and cannabis was associated with an increased risk of experiencing a treatment-related AE in OROS-MPH but baseline use did not increase the risk of SAEs or of any particular category of AE and the adolescents did not experience more treatment-related AEs relative to the adults.
Conclusions: With good monitoring, and in the context of substance abuse treatment, OROS-MPH can be used safely in adolescents with a SUD despite non-abstinence.
Financial Support: National Institute on Drug Abuse, Center for Clinical Trials Network

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EVIDENCE-BASED RESEARCH IN PREGNANT OPIOID-DEPENDENT WOMEN: A COMPARISON OF TWO EUROPEAN SAMPLES.

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Aims: While substance abuse among women of child bearing age continues to be a major public health problem, there is still a lack of randomized controlled studies (RCTs) assessing pharmacological treatment response during pregnancy.
Methods: This investigation directly compares two different European samples of opioid dependent pregnant women (Pilot-study (PS): n=18; European sample of the MOTHER-study: n=41) maintained on either buprenorphine or methadone, using a randomized, double-blind, double-dummy, flexible-dosing study design. Both studies took place at the Medical University of Vienna, Austria. Patients of both trials received vouchers for their attendance and completion of study assessments. Women of the MOTHER-study earned additional vouchers based on drug-negative urine results in an escalating regimen. In both studies morphine drops were administered for the treatment of neonatal abstinence syndrome (NAS) based on modified Finnegan scores.
Results: Participants were prospectively investigated over a mean period of 13.79 weeks in PS and 20.78 weeks in the MOTHER-trial respectively with mean doses at delivery of 14.00mg buprenorphine/52.50mg methadone in PS and 13.44mg buprenorphine/63.68mg methadone in the MOTHER-study. A non-significant higher rate of drop-outs was found in PS compared to the MOTHER-trial. No significant differences between the trials were found in regard to preterm delivery, neonatal weight, length, head circumference as well as NAS treatment duration or total morphine doses. Illicit consumption of opioids and benzodiazepines was significantly higher in PS compared to the MOTHER trial ($p<0.001$).
Conclusions: Early treatment initiation in combination with contingency management for negative urine samples may contribute to better maternal outcome with less maternal illicit substance use during pregnancy.
Financial Support: NIDA grant R01DA018417; educational grant by Schering Plough

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MEPHEDRONE, PATTERNS OF USE, EFFECTS, RISK PROFILE AND ABUSE LIABILITY.

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Aims: To determine the effects, risks and abuse liability of the novel synthetic stimulant drug mephedrone
To determine the impact of legislation on its use in the UK and to assess the utility of biological analysis in confirming its use.
Methods: 2 cross sectional surveys of over 5000 club drug users conducted one year apart in November 2009 and 2010.
In depth telephone risk and effect profiling.
Urine analysis of samples following recent use.
Results: The findings of these studies confirm that mephedrone has an effect profile similar to MDMA but with a duration of action and urge to use profile more similar to cocaine. Users report prosocial stimulant effects with little evidence of aggression and hostility. Users report tolerance and dependence in 20-30% of cases. GCMS can confirm recent use through detection of the parent drug and its major metabolite. Legislation has reduced use but moved distribution to street based dealers. Preliminary follow up results suggest that since banning mephedrone in April 2010 the price has doubled and purity has fallen. The current study appears to suggest that mephedrone will become a staple drug and will be associated with both acute risk and dependence.
Conclusions: Mephedrone is the first stimulant drug to challenge cocaine and MDMA and represents a challenge to legislators, health providers and users. With a high abuse liability, versatile route of administration and as yet poorly controlled precursors, urgent work is required to better define its toxicological risks in man.
Financial Support: EMCDDA $16000 for risk assessment report in 2009

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PROSPECTIVE STUDY OF ADHD AND RISK FOR ADOLESCENT AND YOUNG ADULT DRUG ABUSE.

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Aims: To describe the late adolescent and young adult drug use outcomes from a relatively large, community-identified sample of children with ADHD who have been assessed longitudinally from childhood through late adolescence.
Methods: We present findings from our follow-up assessments at waves 4, 5 and 6 (ages 18 – 22). Three rigorously diagnosed groups that were epidemiologically identified during childhood in 1991: ADHD-externalizing (n=90); ADHD-only (n=29); and matched controls (normals) (n=93). The follow-up battery (T4 – T6) consisted of several standardized measures.
Results: The logistic regression findings at late adolescence (T4; age 18) are generally consistent with the ADHD literature on adolescent drug abuse risk. We observed that the childhood ADHD-externalizing group was associated with outcome; presence of an externalizing disorder (oppositional defiant disorder or conduct disorder) greatly increased the likelihood of adolescent alcohol and cannabis use disorders (AUD and CUD) compared to the ADHD-only and control groups. These findings were found in both boys and girls. At young adulthood (T5 and T6; age 20 and 22), results indicated that childhood diagnostic status was not significantly associated with AUD and CUD risk.
However, ADHD persistence past childhood was associated with outcomes at T4, T5 and T6. ADHD concurrent status at each of these time points was associated with significantly higher rates of AUD and CUD, compared to youth whose ADHD desisted after childhood.
Conclusions: Whereas childhood ADHD without a co-existing externalizing disorder is not associated with an increased risk for drug abuse, as ADHD youth age into young adulthood, we did not find that persistence of ADHD into young adulthood was associated with continued elevated risk for alcohol and cannabis use disorders. This pattern of results was similar in both boys and girls.
Financial Support: This study was supported by grants K02 DA015347 and R01 DA0112995 from the National Institute on Drug Abuse.

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BEHAVIORAL PROFILING OF STIMULANTS AFTER ACUTE ADMINISTRATION IN RATS USING LABORAS™

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Aims: Evaluation of potential abuse liability requires complex tests that are typically carried out in advanced stages of drug development. A simple test that can be used at earlier stages for initial assessment of likely scheduling might improve abuse liability testing. LABORAS™ (Laboratory Behavior Observation, Registration and Analysis System), an automated system that measures locomotor activity along with more refined behavioral elements, was used to profile a number of stimulants either with or without established abuse potential.
Methods: Immediately after s.c. administration of drug, singly housed rats were placed into the LABORAS™ apparatus for a 2hr observation period. A range of behaviours, including grooming, eating, drinking, rearing, locomotor activity, and immobility, were recorded. Stimulants of different pharmacological classes (cocaine, amphetamine, dizocilpine, ketamine, modafinil, caffeine, and nicotine), were evaluated at 3 to 5 doses each, n = 5-8/dose. Drugs were compared to vehicle using ANOVA and post-hoc tests.
Results: Dose-dependent changes across behavioural measures varied between substances, resulting in distinct profiles for each. For example, while locomotor activity and immobility were differentially affected by increasing doses of abused stimulants like cocaine and amphetamine, no such separation was observed with dizocilpine. Decreased grooming was observed with increasing doses of modafinil, but there was little to no effect on locomotor activity or rearing. The inclusion of complementary measures such as onset and time spent eating and drinking faciltiated the characterization of each substance.
Conclusions: Behavioral profiling using LABORAS™ provides a high throughput screening method for an initial evaluation of abuse potential. Comparison of the behavioral effects of novel test substances to the profiles of stimulants with known abuse liability can provide guidance for subsequent evaluation using more specific models such as conditioned place preference, drug discrimination or self-administration
Financial Support: This work was supported by Porsolt

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MAINTAINING MI SKILL PROFICIENCY: AN ENHANCED TRAINING PACKAGE FOR CLINICAL SUPERVISORS PRACTICING IN FRONTIER STATES.

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Aims: Evaluate acquisition of motivational interviewing (MI) skill proficiency among clinical supervisors working in publicly funded substance abuse treatment programs who participated in an enhanced training program.
Methods: Twenty-five clinical supervisors from five frontier states where MI has not been widely disseminated (Colorado, Montana, Nevada, Utah, and Wyoming) participated in an enhanced training that consisted of (1) online instruction; (2) in-person skill-based workshop: (3) submission of a audio taped counseling session demonstrating MI skill proficiency; (4) performance feedback; and (5) follow-up booster sessions if needed to improve skills. Upon successful completion of this enhanced training, participants were invited to attend the advanced MIA:STEP training to prepare them to teach MI to other substance abuse treatment professionals. Clinical supervisors were required to submit an additional audio taped counseling session demonstrating MI skill proficiency prior to acceptance into the MIA:STEP training.
Results: Six months after completing the enhanced training, 85% of the clinical supervisors had maintained their MI skills proficiency, which was determined by independent reviewers who scored clinical supervisors' videotaped counseling session according to the MIA:STEP rating system (Martino, et al., 2007).
Conclusions: Results show that the percentage of clinical supervisors whose tapes did not pass MI proficiency standards was much lower (15%) than reported by Martino, et al. (2007) and others (33%). These findings may offer strategies that address the drift from the research-based interventions (Swain et al., 2010) that frequently occur when attempting to change counselor practices. Although reflective of only a small sample, results may help inform larger studies and could have implications for MI and other EBP training programs. The components and structure of the enhanced training package will be highlighted.
Financial Support: Funded by the Mountain West Addiction Technology Transfer Center

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PUNISHMENT OF COCAINE CHOICE: EFFECTS OF DELAYING PUNISHMENT.

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Aims: Delay to presentation has been shown to decrease the effectiveness of a drug reinforcer, but the effect of delaying the presentation of a punisher of drug self-administration has not been established. The Aims of the present study were: (1) to establish whether a histamine injection could punish cocaine self-administration in a drug-drug choice; and (2) to examine whether delaying the presentation of a punisher would decrease its effectiveness.
Methods: Male rhesus monkeys (n=6) were implanted with double-lumen catheters to allow injection of cocaine via one lumen and histamine via the other. Using a discrete-trials procedure (FR1, timeout 10 min), subjects first chose (20 choices/day) between cocaine (0.05 mg/kg/inj) alone and an injection of the same dose of cocaine followed immediately by an injection of histamine (15-50 μg/kg/inj). After establishing dose-response functions for histamine, monkeys chose between cocaine followed immediately by histamine and cocaine followed by an equal but delayed dose of histamine (delays 3 - 12 min). For this part of the experiment, timeout was increased to 20 minutes to allow testing of relatively long delays.
Results: When choosing between cocaine alone and cocaine followed immediately by histamine, preference varied from indifference at low histamine doses and > 80% choice of cocaine alone as histamine dose increased. When choosing between cocaine followed immediately by histamine and cocaine followed by an equal but delayed dose of histamine, three monkeys preferred the option with delayed histamine. The other three monkeys have, to this point, shown no preference for either option over a similar range of delays.
Conclusions: The results support two conclusions: (1) histamine can function as a punisher in the choice between injections of cocaine; and (2) introducing a delay to a histamine punisher can decrease its effectiveness, at least in some subjects. Delaying punishment of the choice to take a drug can diminish the punisher's effectiveness.
Financial Support: This research was supported by R21-DA-0026832 from the National Institute on Drug Abuse.

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CONJOINT DEVELOPMENT OF ANTISOCIAL BEHAVIORS AND MARIJUANA USE FROM ADOLESCENCE INTO YOUNG ADULTHOOD.

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Aims: Substance use disorders (SUDs) and antisocial behaviors (ASB) frequently co-occur in adolescence, and may persist into adulthood. Optimal characterization of SU and ASB over time can enable identification of clinically-relevant predictors of this persistence. This study characterized the development of ASB and marijuana use (MJU) for individuals with symptoms of ASB and SUD at adolescence.
Methods: Probands originally assessed in adolescence (age 14-18 yrs; mean=15.9) were interviewed in young adulthood (N=241, mean age=21.9, 70% male). Structured clinical interviews (DIS/CIDI-SAM) were used to measure ASB and MJU at adolescence, age 18, age 21, and past year. We used latent growth curve modeling to model individual patterns of change in ASB and MJU over time, and growth mixture modeling (GMM) to identify qualitatively distinct patterns of change.
Results: A parallel process linear growth model was a good fit to the data, $\chi 2(22, N=241) = 34.81$, $p=.04$, CFI=.97, RMSEA=.05. Slopes were significantly negative (p's<.001) for ASB (-.47) and MJU (-.55), indicating decline in both behaviors for the overall sample. Variance estimates for ASB (.14) and MJU (.75) linear slopes demonstrated significant (p's<.001) heterogeneity in individual rates of change over time. The ASB and MJU slopes were positively correlated ($\beta=0.49$, $p<.01$), such that individual rates of change in ASB and MJU tended to be similar in direction and magnitude. In GMM a 3-class solution was the best fit to the data (BIC = 5734.85, Entropy=0.81, LRT p<.01). The three classes were characterized by gradually decreasing ASB with stable low MJU (18.8%), steep decreasing ASB and MJU (28%), and greater initial/gradually decreasing ASB with stable high MJU (53.3%).
Conclusions: The results provide initial identification of distinct developmental patterns of conjoint antisocial behavior and illicit substance use from adolescence into young adulthood. Future studies will identify prognostic indicators of persistent comorbidity of these behaviors.
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YOU'VE GOT DRUGS: ESTIMATING ILLICIT OR INTERNET SALES OF PRESCRIPTION OPIOIDS.

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Aims: Law enforcement and public officials are concerned about illicit sources and Internet sales of abused opioids, but have few tools to estimate which drugs are obtained in this manner and in what quantity. We use tools developed for the DAWN system to examine the correlation between pharmaceutical sales and DAWN ED mentions to estimate illicit sales of opioid pharmaceuticals.
Methods: The manufactured quantities of pharmaceutical dosage forms for common opioids (sustained release, immediate release, combination products) were obtained from FDA records and correlated with the new DAWN data using methods developed and validated for the original DAWN system. The results were then examined for correlations and deviations between the known pharmaceutical quantities for fentanyl, oxycodone, hydromorphone, morphine and hydrocodone and the DAWN ED mentions.
Results: The known amount of strong opioids in the pharmaceutical distribution chain was found to be as highly correlated with new DAWN ED mentions as it was for the original DAWN system. Correlation coefficients of 0.85-0.99 were observed for all drugs in the 2004-2007 period. In 2008, a clear and marked deviation was seen for hydrocodone, indicating an alternative and presumably illicit source for about 20% of the estimated total amount of the drug (both used and abused).
Conclusions: The DAWN system is sufficiently proportional and predictive to allow estimation of supplies of illicit pharmaceuticals from the ED mentions data. Of the opioids analyzed, only hydrocodone appears to have a significant source outside the pharmaceutical distribution system, but that source is a significant fraction of the total.
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EFFECT OF RAT STRAIN AND AMBIENT TEMPERATURE ON THE HYPOTHERMIC AND LOCOMOTOR STIMULANT PROPERTIES OF 4-METHYLMETHCATHINONE.

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Aims: During the last three years, recreational use of the stimulant 4-methylmethcathinone (4-MMC, mephedrone or 4-methylephedrone) has increased dramatically in Europe, particularly the United Kingdom. Some 4-MMC use has also been reported recently in the United States. While there are clinical case reports of adverse reactions following 4-MMC use (e.g., agitation, tachycardia, hypertension and seizures) and the drug has been linked to at least three deaths, there is a paucity of information about 4-MMC pharmacology in the scientific literature. To that end, the studies presented here determined the effect of 4-MMC on thermoregulation and locomotor activity.
Methods: Groups of male Wistar and Sprague-Dawley rats were implanted with radiotelemetric devices and treated with 4-MMC (1-10 mg/kg). These studies were conducted in the dark cycle at both low (23°C) and high (27°C) ambient temperatures
Results: In Wistar rats, 4-MMC induced significant hypothermia at 23°C and 27°C. In contrast, 4-MMC did not reliably reduce body temperatures in Sprague-Dawley rats. In contrast to these strain differences in the hypothermic response to 4-MMC, follow-up trials indicated that the serotonin 1A/7 receptor agonist 8-hydroxy-N,N-dipropyl-2-aminotetralin (8-OH-DPAT) produced similar reductions in body temperature across both groups. Locomotor activity was increased after treatment with 4-MMC in both strains, but the psychomotor effects of 4-MMC were significantly greater in Sprague-Dawley than in Wistar rats. Subsequent challenges demonstrated that 1 mg/kg d-methamphetamine and 10 mg/kg 4-MMC produced indistinguishable levels of locomotor stimulation in both strains of rats.
Conclusions: The results of these experiments indicate that the cathinone analog 4-MMC has a pharmacological profile that is distinct from stimulants like methamphetamine or MDMA.
Financial Support: These experiments were supported by NIH grants R01-DA018418 and R01-DA024705.

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WITHDRAWN

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PRESCRIPTION OPIOID MISUSE: TWO MOTIVATIONAL PATTERNS?

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Aims: Examine the relationship of the Prescription Opioid Misuse Index (POMI) to patients' perceived risks as they reflect motivations for prescription medication misuse.
Methods: The six-item POMI, a five- item Risk Tolerance scale, and questions about perceptions of risk of non-medical use of pain, anxiety, and antidepressant medications and the relative safety of prescription medications were administered to 54 patients prescribed opioids in a pain specialty clinic.
Results: A principal components analysis of the POMI identified two sub-indices. Regression models of the sub-indices on measures of risk tolerance, perceived safety of medications and medication use, and perceptions of risk of medication use without prescriptions revealed two predictive patterns. For one sub-index combining "use more medication than prescribed"","taking pain medicine more often than prescribed", "need early refills", and "taking medication because you are upset", significant predictors were 1) stronger agreement that taking extra medicine when pain is bad is safe and 2) weaker agreement that commercially manufactured drugs are safer than street drugs. For the other sub-index, combining "feel high or get a buzz after using your pain medication" and "ever gone to multiple physicians including emergency rooms to seek prescription refills", significant predictors were greater overall risk tolerance, lower perceived risk of peer disapproval about taking pain medication without prescription, and greater perceived medical risk of taking pain medication without a prescription.
Conclusions: These results provide a refined understanding of the measurement characteristics of the POMI. Further, among pain patients, there may be two different motivations for misuse of pain medication. One motive focuses on the perceived safety of use of extra medication to relieve pain, possibly reflecting self-treatment. The other motive focuses positively on the risks of misuse, possibly reflecting interest in seeking euphoria. The results invite further examination of the POMI to outline the salience of motives for prescription medication misuse.
Financial Support: Carilion Clinic

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32,476: A LOW ADDICTIVE SLOW-ONSET LONG-ACTING DOPAMINE TRANSPORTER INHIBITOR THAT INHIBITS COCAINE'S ACTIONS IN RATS.

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Aims: Agonist replacement therapies have been successfully used for the treatment of opiate and nicotine addiction, but not yet for cocaine addiction. One of the major obstacles is that cocaine-like agonists themselves have strong psychostimulant properties and abuse potential much like those of cocaine itself. In the present study, we investigated a novel slow-onset long-acting dopamine (DA) transporter (DAT) inhibitor – 32,476, as a potential agonist therapy for cocaine addiction.
Methods: Intravenous drug self-administration and in vivo microdialysis with HPLC techniques were used to compare the addictive potential of cocaine and 32,476 by itself, and the pharmacological interactions after co-admionistration.
Results: Systemic administration of 32,476 produced a slow-onset (20-60 min) long-term (6-12 hrs) increase in locomotion and extracellular DA in the nucleus accumbens (NAc). Drug naïve rats self-administered cocaine, but not 32,476. In rats trained to self-administer cocaine, 32,476 maintained significantly lower rates of self-administration and lower progressive-ratio reinforcement break-points than cocaine, suggesting a significantly lower addictive potential for 32,476 as compared to cocaine. Pretreatment with 32,476 significantly inhibited intravenous cocaine self-administration under both fixed-ratio and progressive-ratio reinforcement, shifted the cocaine dose-response self-administration curves downward and to the right, and attenuated cocaine-enhanced extracellular NAc DA, suggesting functional antagonism of cocaine's action after 32,476.
Conclusions: The present findings support further research on 32,476 and similar compounds as potential agonist pharmacotherapies for cocaine addiction.
Financial Support: Supported by NIDA IRP.

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NICOTINE MODULATES EXPRESSION OF DYNAMIN 1 IN RAT BRAIN AND IN SH-SY5Y CELLS.

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Aims: Our previous genetic and proteomic studies demonstrated that dynamin 1 is significantly associated with nicotine dependence (ND) in human smokers and its expression is highly modulated by nicotine in animal brains. To provide further molecular evidence for the involvement of dynamin 1 in the etiology of ND, we investigated the regulatory effect of nicotine on the expression of dynamin 1 using both in vivo and in vitro approaches.
Methods: Adult male Holtzman rats were treated with nicotine in a daily dose of 3.15 mg/kg for 7 days, and the expression of dynamin 1 was measured in seven brain areas. Cultured human SH-SY5Y cells were treated with 1 mM nicotine tartrate, and the expression of dynamin 1 was assessed at different times. Expression was determined by quantitative RT-PCR for RNA and Western blotting for protein.
Results: Dynamin 1 mRNA was significantly down-regulated, by 30%, 31%, and 38%, in the striatum, hippocampus, and medial basal hypothalamus (MBH), respectively, of nicotine-treated rats ($P < 0.01$ for all three regions). Further, dynamin 1 protein was down-regulated by nicotine in the ventral tegmental area (VTA: 39.5%; $P < 0.01$), hippocampus (13.4%, $P < 0.05$), MBH (24.6%, $P < 0.01$), and amygdala (15.7%, $P < 0.05$). In SH-SY5Y cells, dynamin 1 mRNA was significantly down-regulated by nicotine after 1 hour of treatment (51.4%; $P < 0.01$). A consistent decrease in the amount of the protein also was observed after 1 hour of treatment (36.6%; $P < 0.05$).
Conclusions: These results suggest that dynamin1 is highly regulated by nicotine, implying that dynamin 1 may play an important role in neural plasticity induced by nicotine and other drugs of abuse.
Financial Support: This study was supported by National Institutes of Health grants DA-12844 and DA-13783 to MDL, and the Fundamental Research Funds for the Central Universities 2009JBM107 to QX.

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PHYSICIANS' ROLE IN BUPRENORPHINE DIVERSION REDUCTION.

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Aims: One concern in prescribing buprenorphine and buprenorphine/naloxone is to provide effective treatment for opioid dependence while minimizing the misuse and diversion risk. However, little is known regarding the actions and characteristics of prescribing physicians who take steps to reduce diversion.
Methods: Samples of physicians eligible to prescribe buprenorphine were selected from 2008-2009 (N=2,855). Physicians were asked to mark all the steps they took to reduce diversion from a list of 12 pre-specified choices. Differences between the means on questions on specialty, certification, education, training, practice types, and diversion awareness were calculated. Significant measures were included in linear regression where the outcome was the total number of steps taken.
Results: Factors associated with increased number of steps were years certified, years prescribing buprenorphine, number of patients treated, having patients on higher doses, more educational activities taken, awareness of street sales, and concern over diversion as barrier. Specialty, certification, and practice settings were not significantly associated.
Conclusions: Our findings suggest that buprenorphine-related education and experience is important in physicians taking action toward reducing diversion.
Financial Support: This physician survey was supported by a contract from the manufacturer, Reckitt Benckiser Pharmaceuticals Inc. The contract was initially awarded to Wayne State University (Charles R. Schuster, Principal Investigator). In October 2006, the contract was awarded to CRS Associates, LLC (Charles R. Schuster, Principal Investigator). For the analyses for this abstract, Amy Yang was supported by NIDA DA021336 (PI: A.A. Palmer) and DA02812 (PI: H. de Wit).

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ALCOHOL'S EFFECTS ON BEHAVIORAL INHIBITION, RISK-TAKING, AND SUBJECTIVE EFFECTS IN HUMAN MODERATE TO HEAVY DRINKERS.

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Aims: The current study investigated two hypothesized acute effects of alcohol which may contribute to excessive drinking: impaired behavioral inhibition and increased risk-taking.
Methods: 17 moderate to heavy drinkers completed two sessions: alcohol (0.35 g/kg) and placebo (0.04 g/kg), order counterbalanced, double blind. Drinks were administered at timepoints 1, 2, and 3, and each assessment was completed at each of timepoints 0 through 5 (each separated by 1 h). Subjective effects scales measured subjects' ratings on several questions about drug-related sensations. In a cued go/no-go task, cues were 70% predictive of the upcoming targets. Failures of inhibition were recorded when a response was made during a no-go target. A risky-choice task measured choices between gaining 5 cents or gambling on a variable outcome.
Results: Blood-alcohol level peaked at timepoint 3 (mean[SD]: 0.011[0.035]). In the cued go/no-go task, there was a significant interaction between timepoint and alcohol condition on the number of false alarms ($p=0.001$). Post-hoc tests revealed that alcohol increased false alarms relative to placebo at timepoints 3 and 4 only. There was a significant interaction between alcohol condition and timepoint on ratings of "Do you feel any drug effects?", "Do you like the effects?", and "Are you high?" (for all, $p<0.001$). Ratings of "Do you want more of what you consumed?" differed under alcohol vs. placebo within each timepoint, indicating an alcohol-priming effect. On the risky-choice task, the percentage of risky-option choices varied in accord with predictions based on the expected value, but alcohol effects were not systematic.
Conclusions: These results showed that alcohol impairs moderate to heavy drinkers' behavioral inhibition at doses for which risk-taking was unaffected, indicating a dissociation in the susceptibility to alcohol for the processes underlying these two types of problematic behavior.
Financial Support: T32 AA007468.

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THE LONG-ACTING ALPHA-1 ANTAGONIST, DOXAZOSIN, ALTERS COCAINE'S EFFECTS IN RATS.

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Aims: Pharmacologically manipulating norepinephrine (NE) neurotransmission alters the behavioral effects of cocaine. Previously we showed that the short-acting alpha-1 adrenergic antagonist prazosin blocks cocaine reinstatement of self-administration. Here we tested the long-acting alpha-1 adrenergic antagonist doxazosin (DOX) on cocaine locomotor (LOCO) sensitization, elevated plus maze (EPM), and effects on cyclic-AMP-response-element-binding protein (CREB) and tyrosine hydroxylase (TH) protein levels in the nucleus accumbens (NAc) and caudate putamen (CP).
Methods: Rats (n=7-8) were habituated to the LOCO apparatus then administered either saline, cocaine (COC, 10mg/kg) or DOX (0.3mg/kg) alone or in combination for 5 days (60-min/day). After 10-days of drug withdrawal, all rats were administered COC (10mg/kg), and LOCO activity was again assessed. These same drug combinations were also tested in the EPM. Thirty-min after EPM testing rats were sacrificed and brains assessed for CREB and TH protein levels in the NAc and CP.
Results: COC increased LOCO activity across days indicating sensitization. The effect of DOX alone was similar to saline. COC+DOX combination increased activity above COC alone on day 1 ($p=0.07$) but decreased activity on days 4 and 5 ($p<0.05$). COC challenge on day 10 withdrawal increased LOCO activity in all previously drug-treated groups compared to saline ($p<0.01$). COC-induced activation was lower in rats treated with COC+DOX ($p<0.05$). COC increased time spent on open arms and decreased time in the closed arms of the EPM, effects that were blocked by DOX. COC and DOX alone increased CREB and TH protein levels in the NAc and CP. DOX attenuated COC-associated increases in CREB protein to saline levels whereas increases in TH were also blocked but greater than saline ($p<0.05$).
Conclusions: These results are consistent with previous studies indicating that the NEergic system, alpha-1 receptors in particular, are vital to cocaine's behavioral and biochemical effects.
Financial Support: DA 020117

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RELATIONSHIP BETWEEN IMPULSIVITY AND AMPHETAMINE CONDITIONED PLACE PREFERENCE.

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Aims: Impulsivity has been linked to increased drug abuse vulnerability in adolescents and young adults. Individuals who are impulsive are more likely to use and abuse drugs compared to individuals who are self-controlled. The present preclinical study was designed to determine if a correlation exists between impulsivity and amphetamine conditioned place preference (CPP).
Methods: Fifty-four Sprague Dawley rats were first trained in a delay discounting task, in which rats chose between a small, immediate reward and a larger, delayed reward. Animals that demonstrated the strongest preference for the small immediate reward were designated as impulsive. Rats were then tested for amphetamine CPP in which injections of either amphetamine (0.1, 0.5, or 1.5 mg/kg) or saline were paired with one side of a CPP chamber. Following conditioning, preference scores were determined by allowing the rat free access to both end compartments, and these preference scores were correlated with the scores obtained from the delay discounting task.
Results: Rats high in impulsivity spent more time in the compartment paired with amphetamine compared to those low in impulsivity following 0.5 mg/kg amphetamine.
Conclusions: The results suggest that impulsivity may be related to differential sensitivity to amphetamine reward, thus implicating individual differences in impulsivity on vulnerability to stimulant abuse.
Financial Support: NIH grant P50 DA05312.

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FUTURE, PAST, PROBABILITY, AND SOCIAL DISCOUNTING BY ACTIVE METHAMPHETAMINE USERS.

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Aims: The purpose of this study was to (1) comprehensively compare various forms of discounting by methamphetamine (MA)-dependent individuals and non-using controls, and to (2) explore relationships between the forms of discounting.
Methods: Thirty (30) currently MA-dependent and twenty nine (29) controls completed the study. Computerized assessments were completed for future, past, probability, and social discounting of rewards, at $50 and $1,000 magnitudes. Discounting parameters were calculated using nonlinear regression on obtained indifference points according to the exponential-power discounting model. Group comparisons were conducted via parametric analyses with relevant demographic variables included as covariates. Relationships between assessments were explored with Pearson correlations.
Results: Greater discounting of future and past rewards by active MA-dependent individuals was observed, compared to controls. No difference was observed between groups on measures of probability discounting. Greater social discounting by MA-dependent individuals was observed, but only in the small ($50) magnitude condition. Correlations revealed strong positive relationships (1) between small and large magnitudes, and (2) future and past conditions. No systematic patterns of significant correlations were observed between other discounting conditions.
Conclusions: Consistent with the extant literature on other forms of drug dependence, the present results confirm that actively MA-dependent individuals discount future and past rewards more than those who do not use MA. Additionally, the results replicate the relationship between future and past discounting. The results further suggest that groups do not differ on probability discounting, but may differ on social discounting.
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INTER-TEMPORAL CHOICE AMONG METHAMPHETAMINE-DEPENDENT VOLUNTEERS: COMPARISON OF IMMEDIATELY AVAILABLE MONEY VS. METHAMPHETAMINE.

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Aims: Inter-temporal choice (ITC) studies have provided valuable insights into drug-dependence and other impulsive disorders. Drug-dependent volunteers reliably exhibit greater impulsivity as indicated by greater discounting of delayed rewards across a wide variety of drugs of abuse including methamphetamine (MA) when compared to matched controls. Typically, drug-dependent volunteers exhibit greater discounting for their drug of choice relative to equivalent values of money. To our knowledge, no studies have directly compared discounting of money when the immediately available commodity is money vs. MA in MA-dependent volunteers.
Methods: MA-dependent volunteers (N=37, to date) were exposed to two ITC tasks for hypothetical rewards. In the money vs. money task (M-M), participants made repeated choices between various amounts of money (between $0 and $1,000) available immediately vs. $1,000 after a fixed delay. The MA vs. money task (MA-M) was identical in format except that the immediate choice was MA (valued between $0 and $1,000). In both cases, fixed delays ranged from 1 d to 25 yrs. Data were fit to Mazur's hyperbolic discounting equation in order to solve for the discounting rate k.
Results: The geometric mean k-value for the M-M task was 1.1x10-2 days-1, which translates to $1,000 discounted to $500 after a .25 yr delay. As a point of comparison, studies utilizing similar procedures in cigarette smokers and cocaine-dependent volunteers report similar decreases after 2.3 and .45 yrs, respectively. Significantly greater discounting (p=.008) was observed in the MA-M task, with $1,000 deemed to be equivalent to $500 worth of MA after .03 years.
Conclusions: MA-dependent volunteers exhibited relatively greater discounting compared to other stimulant-dependent populations. To our knowledge, the current study is the first to report significantly greater discounting when MA was available immediately vs. money.
Financial Support: Supported by NIH grant R01DA023468

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THE IMPACT OF CANNABIS USE ON COGNITIVE FUNCTIONING IN PATIENTS WITH SCHIZOPHRENIA.

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Aims: Cannabis use is highly prevalent among people with schizophrenia and, coupled with impaired cognition, is thought to heighten the risk of illness onset. However, while heavy cannabis use has been associated with cognitive deficits in long-term users, studies among patients with schizophrenia have been contradictory.
Methods: This article consists of two studies. In Study I, a meta-analysis of 10 studies comprising 572 patients with established schizophrenia (with and without comorbid cannabis use) was conducted. In Study II, we examined the neuropsychological performance of 85 patients with first-episode psychosis (FEP) and 43 healthy non-using controls.
Results: Study I: Patients with a lifetime history of cannabis use had superior neuropsychological functioning. Study II: Relative to controls, FEP patients with a history of cannabis use (FEP+CANN; n=59) displayed only selective neuropsychological impairments while those without a history (FEP-CANN; n=26) displayed generalized deficits. When directly compared, FEP+CANN patients performed better on tests of visual memory, working memory, and executive functioning. Patients with early onset cannabis use had less neuropsychological impairment than patients with later onset use.
Conclusions: These findings suggest that patients with psychosis who have a history of cannabis use have superior neuropsychological functioning compared to non-using patients. This association between better cognitive performance and cannabis use in schizophrenia may be driven by a subgroup of 'neurocognitively less impaired' patients, who only developed psychosis after a relatively early initiation into cannabis use.
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DO THE OFFERED HARM REDUCTION INTERVENTIONS MEET THE NEEDS OF HIGH-RISK DRUG USERS? FACTORS INFLUENCING ACCEPTANCE OF TREATMENT PROGRAMS.

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Aims: Problematic drug use (PDU) presents a major public health concern due to high-risk behaviors of drug users such as intravenous drug use, unprotected sex, and illegal activities. The aims of the study were to describe the characteristics of high-risk opiate users (HROUs) in Vienna and to investigate their needs and treatment satisfaction in order to identify predictors for acceptance of treatment programs and retention in therapy.
Methods: Face-to-face interviews were conducted using a structured questionnaire (including parts of Maudsley Addiction Profile, European Addiction Severity Index, Treatment Perception Questionnaire and the WHO-Disability Assessment Schedule) with N=153 HROUs from two target groups: 1) HROUs in opioid maintenance treatment with concomitant drug use (MT n=103), 2) HROUs not in treatment (NIT n=50).
Results: A significant reduction of drug use (p<.000) and improvement of somatic (p=.001) and psychiatric (p=.011) symptoms were observed in the MT group. Psychosocial counseling (p=.007), improvement in interpersonal relationships (p=.010), employment (p=.010), and absence of criminal behavior (p=.007) were identified as predictors for the treatment satisfaction.
Conclusions: The findings emphasize the efficacy of a multidisciplinary treatment approach facing the complexity of negative consequences of substance use disorders. Only individually tailored treatment meeting the needs of the HROUs seems to improve perceived quality of life and treatment satisfaction as well as retention in therapy.
Financial Support: This research was supported by the European Commission-contract number QLG4-CT-2002-01681 (Fifth Framework Programme).

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IMPULSIVITY, AFFECTIVE STATE, AND COGNITIVE PERFORMANCE IN HEROIN-DEPENDENT INDIVIDUALS IN GUANGDONG, CHINA.

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Aims: To explore relationships between impulsive personality traits, affective state, and cognitive performance in heroin dependent individuals and controls.
Methods: We evaluated a sample of heroin dependent individuals residing for ≥1 month in compulsory rehabilitation centers (n=100) and a sample of age and gender matched, non-drug using controls(n=98)in Guangdong province, China. All participants were assessed using the Barratt Impulsiveness Scale (BIS), Sensation Seeking Scale (SSS); Chinese Scale of Affect (CAS) which assess current positive and negative mood, Hospital Anxiety and Depression Scale(HADS)for assessing the severity of anxiety and dpression; Assessments of working memory, decision making, inhibition control and problem solving, included a modified n-back task, Iowa Gambling Task(IGT), Continuous Performance Task (CPT),and Wisconsin Card Sorting Test(WCST).
Results: Heroin dependent individuals reported lower positive affective state, higher negative affective state and higher depression on CAS and HADS; higher impulsivity on both SSS and BIS ($p<.01$ for all comparisons). Greater impulsivity and lower affective state were associated with impaired performance on some of the cognitive tests for both heroin users and controls. Education level differed significantly between heroin dependent individuals and controls and was strongly associated with cognitive task performance.
Conclusions: Heroin dependent individuals showed greater impulsivity, lower affective state and higher depression, all of which negatively affect cognitive performance. Evaluation of the effects of heroin dependence history on cognitive performance testing is complicated by the educational differences between heroin dependent individuals and controls. Further studies are needed to explore the potential cognitive impairments in heroin dependent individuals in China.
Financial Support: Supported by Guangdong 211 key project funding (project number:50621070)from Guangdong Goverment,China.

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SOCIAL INTERACTION- VS. COCAINE CONDITIONED PLACE PREFERENCE IS ASSOCIATED WITH A DIFFERENTIAL ACTIVATION OF NUCLEUS ACCUMBENS SHELL CHOLINERGIC INTERNEURONS.

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Aims: Using findings by WE Pratt and AE Kelley (2004, 2007), our in vivo microdialysis data (Crespo et al. 2006 J Neurosci 26, 6004), and employing a highly sophisticated optogenetics approach, K Deisseroth and coworkers (Witten et al. 2010, Science, in press) plausibly identified nucleus accumbens cholinergic interneuron activity as necessary for the acquisition of cocaine conditioned place preference (CPP). We could in the meantime demonstrate that social interaction with a weight- and gender-matched male conspecific is able to reverse cocaine CPP in rats despite continuing exposure to cocaine (Fritz et al. 2010, Addiction Biology, in press), an effect that is dose-dependently enhanced by the sigma1 receptor antagonist BD1047 (Fritz et al. 2010, Pharmacology, in press). The present study was designed to investigate whether social interaction CPP is associated with an AcbSh ACh release pattern that is different from that engendered by cocaine CPP.
Methods: Adult (6 wk) Sprague Dawley rats were trained for CPP to either 15 mg/kg i.p. cocaine or social interaction with a weight- and gender-matched conspecific.
Results: In vivo microdialysis before vs during vs after the 15-min CPP test revealed the following AcbSh ACh release [fmol/(15-min sample)]: For cocaine CPP (N=9), 1695 ± 552 vs 4723 ± 1862 vs 1747 ± 679 and for social interaction CPP (N=8), 13036 ± 3645 vs 3133 vs 1421 vs 1052 ± 270. AcbSh ACh release in naive rats (N=8) subjected to the same context and CPP test procedure was 1255 ± 339 vs 603 ± 156 vs 652 ± 91 fmol/(15-min sample).
Conclusions: Our findings suggest that accumbens shell ACh interneuron activity is differentially affected by contextual stimuli associated with social interaction vs contextual stimuli associated with cocaine.
Financial Support: FWF M1169-B18, FWFP18787-B05 and VEPPP.

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ORBITAL FRONTAL CORTEX ACTIVITY PREDICTS EXECUTIVE COGNITIVE FUNCTIONING IN EARLY ADOLESCENTS.

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Aims: During adolescence, development of brain regions underlying reinforcement processing and immaturities in executive cognitive functioning (ECF) contribute to the risk of substance use disorder (SUD). The orbital frontal cortex (OFC) regulates emotional processes of ECF, particularly in response to reward. The OFC supports inhibition of disadvantageous prepotent behavior for more profitable behavior. Studies indicate that OCF is an important neurobiological target in addiction. ECF, through response inhibition, and OFC development represents a neuropsychological mechanism whereby dysmaturation in adolescence may predispose individuals to SUD outcomes. However, few studies assess the role of OFC in ECF-related factors of SUD risk in adolescents. This study aims to determine the relationship between OFC activity, response inhibition, and ECF impairment in adolescents.
Methods: Participants, 61 (50.8% male) adolescents (ages 12-15 years) prior to significant substance use, were recruited by random digit dialing and assessed as part of a study on adolescent brain development and risks for SUDs. We examined OFC activity during response inhibition with an fMRI antisaccade task that required inhibition of prepotent oculomotor responses in varying reward contexts. We correlated OFC activation with scores on the BRIEF: Global Executive Composite (GEC) scale, where higher scores reflected greater ECF impairment.
Results: The OFC showed a significant condition effect with greater activation in trials preceded by a reward condition cue. Additionally, scores on the GEC were positively correlated with OFC activation.
Conclusions: Results confirm previous studies that indicate OFC regulation of reward relevant behavior by demonstrating greater activity in reward contexts. Correlation between OFC activation and GEC score suggests that impaired individuals exhibit more effortful performance in response inhibition. This extends findings in OFC involvement in behavioral regulation to other ECF constructs during adolescence.
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NIDA P50DA05605

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CONTINGENCY MANAGEMENT AT A MMT CLINIC IN SHANGHAI, CHINA.

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Aims: To explore whether addition of CM improves treatment outcomes at a community-based MMT clinic in Shanghai, China.
Methods: 60 heroin dependent patients entering MMT were randomized into MMT only (MMT group; n=30) or MMT plus CM (CM group; n=30) and followed for 6 months. Patients assigned to CM could earn chances to play a computerized video game similar to a fishbowl prize draw method, contingent on opiate-negative urine tests (1 per week) and medication adherence (3 uninterrupted days of methadone adherence) during the first 12 weeks of study. Primary outcome measures included methadone adherence and opiate abstinence.
Results: Neither demographic characteristics or substance use variables differed significantly between two groups. There were no significant differences between CM and MMT groups on planned outcome measures: percentage of days receiving methadone (67% vs. 66%), longest duration of full daily methadone adherence during the 6 months (62 vs. 52 days), and maximum consecutive weeks of opiate abstinence during the first 12 weeks (7.6 vs. 6.4 weeks). The proportion of opiate-negative urine tests (a secondary outcome measure), aggregated in 3 successive 4-week intervals, was higher for patients treated with CM ($p<.05$).
Conclusions: We found that addition of CM to MMT does not substantially improve treatment outcomes at a community-based MMT clinic in Shanghai. Although CM group had greater opiate use reductions than MMT group, participants in both groups of this study showed very fast decrease in drug use in the first 4 weeks of treatment and maintained low rates of illicit opiate use in the following 8 weeks of the study. This pattern of outcomes is not common in patients receiving MMT in China. Further studies with larger samples are necessary to investigate the effectiveness of CM in MMT in China.
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DEVELOPMENT OF BIVALENT LIGANDS FOR THE CB1-OREXIN 1 RECEPTOR HETERODIMERS.

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Aims: CB1 and orexin 1 receptors have been shown to readily form receptor heterodimers in vitro, and display altered receptor trafficking and function. Furthermore, these receptors are colocalized in certain brain regions, and functional cross-talk between CB1 and OX1 receptors has been demonstrated in vivo. However, the in vitro and in vivo pharmacology of these heterodimer targets has to be further studied in order to recognize and take full advantage of the potential therapeutic utility of their modulation. One means of achieving this objective is to develop bivalent ligands that preferentially interact with CB1-OX1 heterodimers and demonstrate their selectivity for heterodimers in vitro.
Methods: Bivalent ligands, composed of a SR141716 unit and an ACT-078573 moiety linked by spacers of various lengths, and the corresponding monovalent controls were designed and synthesized. The functional activities of these ligands were determined using intracellular calcium mobilization assays at the CB1 and the OX1 receptors, respectively. Target compounds were then further evaluated in calcium assays using cells cotransfected with the CB1 and OX1 receptors.
Results: A number of compounds demonstrated Ke values that were pharmacologically relevant in the nanomolar range in these assays. Enhancement of potency was observed for several bivalent ligands in the cells cotransfected with CB1 and OX1 receptors compared to the individual cells.
Conclusions: We have synthesized a series of bivalent and monovalent ligands featuring SR141716 and ACT-078573 and characterized them using a calcium mobilization functional assay in individual cells and cells cotransfected with both CB1 and OX1 receptors. Several compounds showed nanomolar potency in the calcium mobilization assay. These novel compounds may assist the probe of the function and mechanism of receptor dimerization and further elucidate their physiological roles.
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SEX DIFFERENCES IN OREXIN MEDIATION OF LOCOMOTION AND COCAINE-SEEKING IN RATS.

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Aims: Prior studies have demonstrated sex differences in locomotor and reward-associated behaviors with cocaine. The orexin/hypocretin system has recently been implicated in the conditioned-cued reinstatement of cocaine-seeking in male rats. Although female rats express higher levels of orexin A peptide and orexin 1 receptor (OX1R) than males, it is unknown if the orexin system shows sexual dimorphism in response to cocaine-seeking. In this study, we assessed the effects of the selective OX1R antagonist, SB-334867 (SB), on locomotion and reinstatement of cocaine-seeking.
Methods: All male and female rats were administered SB (10, 20, or 30 mg/kg, i.p.) or vehicle 30 min prior to tests. Rats were first tested for basal and acute-cocaine (10 mg/kg, i.p.) induced locomotion. Subjects then experienced daily sessions (2 hr/day for 10 days) of lever pressing for cocaine (0.6 mg/kg/infusion, i.v.) paired with stimulus cues, followed by daily extinction trials for 7 days. On test days, reinstatement of cocaine-seeking was triggered by cocaine-paired cues, the pharmacological stressor, yohimbine (2.5 mg/kg, i.p.; 15 min prior to test), or yohimbine+cues in a counterbalanced order.
Results: In males, 20 and 30 mg/kg SB reduced basal locomotion; cocaine-induced hyperlocomotion was blocked by all three doses. In females, only the 20 mg/kg SB reduced basal and cocaine-induced locomotion. SB significantly attenuated cue-induced reinstatement in males, but not females, while SB decreased yohimbine and yohimbine+cue induced reinstatement in both males and females.
Conclusions: These data suggest that male rats are more sensitive to the effects of OX1R blockade for locomotion than females. Although stress-mediated cocaine-seeking was under the control of the orexin system in both male and female rats, orexin regulation of cue-induced cocaine-seeking occurs only in males, but not females. A greater understanding of sex differences in the orexin system will lead to potential new treatments for cocaine addiction, including gender-specific approaches.
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INVOLVEMENT OF V1B AND KAPPA OPIOID RECEPTORS IN HPA HYPERACTIVITY DURING ACUTE WITHDRAWAL FROM CHRONIC COCAINE EXPOSURE IN RODENTS.

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Aims: Central arginine vasopressin (AVP) plays an important role in regulation of the HPA axis, and stress-related anxiogenic and social behavior. AVP and dynorphin are co-expressed in the PVN of the hypothalamus. We have recently reported that acute cocaine withdrawal increased AVP mRNA levels in the PVN and elevated HPA hormones in rats, which persisted into prolonged withdrawal. In this study, we first determined the effect of pharmacological blockade of the V1b receptor or kappa opioid receptor (KOP-r) on HPA activation in acute withdrawal (1-3 days) from 14-day "binge" escalating dose cocaine in rats. We also examined several subpopulations of hypothalamic AVP neurons, including PVN after acute cocaine withdrawal in mice.
Methods: Chronic escalating-dose (45 mg/kg on day 1 up to 90 mg/kg on day 14) "binge" cocaine administration, followed by acute (1 day) or chronic (14 days) withdrawal. AVP gene expression was measured in AVP-eGFP promoter transgenic mice, in which AVP neurons are labeled with eGFP.
Results: Pretreatment with either the highly selective V1b antagonist SSR149415 or KOP-r antagonist norBNI (but not naloxone) significantly attenuated the elevation of plasma ACTH and corticosterone (CORT) levels during acute cocaine withdrawal. Immunohistochemistry showed about 90% colocalization of AVP-immunoreactivity with eGFP-expressing neurons, and single-cell RT-PCR amplified AVP mRNA in eGFP+, but not eGFP-, neurons. Similar increases in plasma CORT levels after acute withdrawal were observed in both eGFP+ and eGFP- mice. Acute cocaine withdrawal increased the numbers of AVP-eGFP neurons in the parvocellular division of PVN only.
Conclusions: Our results suggest that during acute withdrawal from chronic escalating-dose cocaine, (1) an enhanced AVP promoter activity was found in the PVN (as reflected by greater numbers of AVP-eGFP neurons), with HPA hyperactivity; and (2) an involvement of V1b and KOP-r receptors in modulation of HPA activity.
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WHEEL RUNNING AFFECTS ESCALATION OF COCAINE INTAKE IN ADOLESCENT AND ADULT FEMALE RATS.

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Aims: Concurrent access to an exercise wheel has been shown to reduce cocaine self-administration under maintenance conditions and to suppress cocaine-primed reinstatement in adult rats. In the present study, the effect of wheel running on the escalation of cocaine intake during long access (LgA) conditions was assessed.
Methods: Adolescent (N = 12) and adult (N = 13) female rats were allowed to acquire wheel running and establish a running baseline over 3 days. Rats then were catheterized and allowed to self-administer cocaine (0.4 mg/kg, iv) during 6-hr daily sessions for 16 days with concurrent access to either an unlocked or a locked wheel during each session. Subsequently, for 10 additional sessions, wheel access conditions during cocaine self-administration sessions were reversed (i.e., locked wheels became unlocked and vice versa).
Results: Preliminary results indicate that unlocked wheel access may be more effective at attenuating cocaine intake in adolescent compared to adult female rats. Concurrent access to an unlocked exercise wheel decreased responding for cocaine and attenuated escalation of cocaine intake irrespective of when access occurred. However, when the wheel was subsequently locked for groups with initial access to an unlocked wheel, cocaine intake increased.
Conclusions: Wheel running was sufficient to reduce cocaine intake during LgA conditions, but concurrent access to running was necessary. Rat models suggest that exercise has the potential to be a useful intervention to reduce cocaine-seeking behavior and may be more effective in adolescents than adults.
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GENDER AND CANNABIS USE: IS THERE EVIDENCE OF 'TELESCOPING'?

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Aims: Past research on gender differences in the development of substance use disorders has identified a 'telescoping effect' in which females, despite initiating substance use at a later age than males, progress to chronic use and/or dependence at a faster rate. However, more recent work has failed to find evidence of such an effect. The current ongoing study is designed to investigate gender differences in the progression from initial use of cannabis to problematic use patterns in adult cannabis users.
Methods: At this time a total of 139 (81 male, 58 female) participants has responded to newspaper ads for recreational marijuana users to take part in several human laboratory studies of cannabis use. The screening battery includes the BDI-II, a medical history and physical exam, a Drug Use Questionnaire, and a semi-structured psychiatric interview.
Results: Participants ranged in age from 21 to 45 (M = 28.44 ±5.69) and were predominantly African American (84%). Data from 128 participants who completed the screening process indicate that the majority met DSM-IV diagnostic criteria for cannabis dependence (76.2%; N = 99), while 16.9% met diagnostic criteria for cannabis abuse, current (N = 22). One-way ANOVAS were conducted to examine whether males and females significantly differed in age of onset of cannabis use, age at first regular (defined as 3 times a week or more) cannabis use, age at first daily cannabis use, as well as the latency from initiation of use to daily use. Results indicated that females had a higher mean age at first use, at regular use, and at daily use; however, the mean latency from first use to daily use and rates of abuse/dependence did not differ significantly as a function of gender.
Conclusions: Overall, these preliminary results from our largely urban and African American sample did not support the existence of a telescoping effect in cannabis use as females appear to progress to daily cannabis use at a similar rate to males despite a later age at onset of use.
Financial Support: Supported by NIDA R01DA026761, R21DA026761, and Joe Young, Sr. funds from the State of Michigan.

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KNOWLEDGE OF HIV TRANSMISSION THROUGH BREAST MILK AMONG DRUG-DEPENDENT PREGNANT WOMEN.

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Aims: To identify correlates of having correct knowledge of HIV transmission through breast milk among drug dependent pregnant women
Methods: Data for this study came from the baseline assessment of a larger study aimed at adapting an integrated family and cognitive-behavioral HIV prevention intervention (IFCBT-HIVPI) manual for use with drug dependent pregnant women. Women were asked about whether HIV is transmitted through breast milk and were considered to have correct knowledge if they answered "Yes" to the question, and were considered to lack correct knowledge if they answered "No" or "I Don't Know". Our final analysis included data from 97 women. We used frequencies to summarize sociodemographic characteristics, and then chi square tests and t-tests to identify significant differences between women who did and did not have correct knowledge about HIV transmission through breast milk. We then used simple and multivariate logistic regressions to calculate odds ratios, adjusted odds ratios and 95% confidence intervals for having correct knowledge.
Results: When asked whether HIV could be transmitted through breast milk, 72 women (74.22%) answered correctly. After controlling for demographic variables, black women were 1.78 times more likely than white women to have correct knowledge (95% CI 1.06-3.00; p=0.03). Additionally, when compared to women who did not smoke crack during the last six months, women who did smoke crack had 0.15 times the odds of having correct knowledge (95% CI 0.04-0.59; p<0.001).
Conclusions: White women and women who smoke crack are the most likely to be lacking knowledge about HIV transmission through breast milk. Given that HIV risk behaviors are common among this population, there is an urgent need to develop and implement interventions targeting these subgroups of drug dependent pregnant women in order to prevent HIV transmission to their children.
Financial Support: This study was supported by NIDA grant R01DA020929 and T32DA007292 funding.

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MOTIVATIONAL ENHANCEMENT AND MINDFULNESS MEDITATION FOR YOUNG ADULT FEMALE MARIJUANA USERS.

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Aims: Test the feasibility and effectiveness of a brief intervention that combines motivational enhancement (ME) with mindfulness meditation for marijuana cessation among young adult females with comorbid anxiety symptoms. We hypothesized that our intervention group would show greater decreases in marijuana use at follow-up.
Methods: A total of 34 participants were enrolled in this pilot study. Participants were females between the ages 18-30 that have used marijuana at least 3 times in the past month; expressed a desire to quit/reduce marijuana use; and reported marijuana use associated with the relief of anxiety symptoms. Participants were randomized (2:1 ratio) to either the intervention group (n=22) consisting of 2 sessions of ME plus mindfulness meditation or an assessment only control group (n=12). Participant's marijuana use was assessed at baseline, 1, 2, and 3 months post-treatment. Fixed-effects regression modeling was used to analyze the treatment effects.
Results: On average participants reported using marijuana on 17.7 (± 9.1) of the 30-days prior to baseline. The intervention arms did not differ significantly with respect to demographic characteristics, baseline marijuana use, or loss to follow-up. Compared to controls, those randomized to the intervention showed significantly less days of marijuana use during follow-up ($\chi 2=8.89$,df=3,p=.031). Specifically, those randomized to intervention used marijuana on 6.15 (z=-2.42,p=.015), 7.81 (z=-2.78,p=.005), and 6.83 (z=-2.23,p=.026) fewer days at months 1, 2, & 3, respectively, than controls.
Conclusions: Findings from this study provide preliminary evidence for the effectiveness of a brief ME plus mindfulness intervention for young adult female marijuana users with comorbid anxiety symptoms. These findings may suggest that our combined intervention offers an alternative method for reducing anxiety related symptoms.
Financial Support: Internal funds of Butler Hospital were used to fund this study.

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EFFECTS OF ALCOHOL ON THE PHARMACOKINETICS OF REMOXY®, AN EXTENDED-RELEASE FORMULATION OF OXYCODONE, IN HEALTHY VOLUNTEERS.

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Aims: A need exists for extended-release (ER) opioids that resist manipulation leading to dose-dumping thereby causing the release of potentially fatal drug doses. Alcohol consumption with opioids occurs often, despite contraindications, representing a significant concern due to the potential for pharmacokinetic (PK) interactions and combined depressive effects on the central nervous system. Remoxy® (King Pharmaceuticals, Inc., Bristol, TN) is a water-insoluble, highly-viscous, oral formulation of ER oxycodone developed to resist common methods of physical manipulation and chemical challenge. This phase I, randomized, open-label, 4-way crossover study evaluated the rate and extent of absorption of Remoxy administered with ethanol in healthy volunteers.
Methods: Subjects were randomized to 1 of 4 treatment sequences (Remoxy 40 mg plus water, 4%, 20%, or 40% ethanol), each separated by a 96-h washout period. Plasma samples were collected at specified intervals. PK parameters were calculated using non-compartmental analyses. Safety was monitored throughout the study.
Results: 37 subjects received ≥1 dose of study drug. Across treatment groups, mean values for C_{max} and AUC were similar, except for a lower C_{max} for Remoxy plus 20% ethanol and a slightly higher (~10%) C_{max} for the Remoxy plus 40% ethanol, relative to water. For the latter treatment, confidence intervals for total exposure were slightly above the accepted 80%–125% limits for bioequivalence. This difference, however, was small compared with the multiple-fold C_{max} increases typical of dose dumping. Remoxy was well tolerated with no serious adverse events; most adverse events were related to alcohol intolerance.
Conclusions: These data indicate that coadministration of Remoxy with alcohol does not have a clinically significant effect on oxycodone PK and provide evidence that the highly viscous Remoxy formulation resists dose dumping of the drug when coadministered with up to 40% alcohol.
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