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### ESTROGEN INCREASES BEHAVIORAL RESPONSES TO CARRAGEENAN-INDUCED INFLAMMATION IN OVARECTOMIZED MICE.

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**Aims:** Estrogen decreases nociceptive responses in inflammatory models of hyperalgesia in rats. Because of the importance of murine models, the aim of this study was to determine if estrogen affects inflammation-mediated nociceptive behavior in mice as well.

**Methods:** To this end, sixty 10-week old ovariectomized (OVX) C57BL mice were implanted with Silastic capsules containing 0% (cholesterol), 10%, 20%, 30% or 40% 17 $\beta$ -estradiol. Latency to hindpaw flinching in response to a medium (4.9mV) heat stimulus was measured using a Hargreaves' PAW thermal stimulator prior to and at 1 and 5 hours after injection of carrageenan (1% injection into the intraplantar region of the right hind paw).

**Results:** In the injected paw, there was a time effect; latencies at 1 and 5 hours post-injection were significantly shorter than those at baseline ( $F(2)=26.0531$ ,  $p<0.001$ ). Further, estrogen lowered latencies to paw withdrawal in both injected ( $F(4)=5.8956$ ,  $p<0.001$ ) and non-injected paws ( $F(4)=13.0874$ ,  $p<0.001$ ).

**Conclusions:** Thus, estrogen significantly increases pain sensitivity to inflammation in both injected and non-injected paws over time in mice, contrary to what has been previously shown in rats. Understanding the mechanisms of a potentially important consequence of estrogen-alone therapy may provide new insights into the treatment of injury-induced pain in women (post-menopausal and young hypoestrogenic) who are receiving estrogen-alone therapies.

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### A BIVALENT LIGAND (MDAN-21) CONTAINING $\mu$ -AGONIST AND $\delta$ -ANTAGONIST PHARMACOPHORES IS DEVOID OF SIGNIFICANT PHYSICAL DEPENDENCE CAPACITY IN RATS.

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**Aims:** Aims: MDAN-21 was found to be 50 times more potent than morphine as an analgesic. Of special significance, antinociceptive tolerance, conditioned place preference and reinstatement were not observed in mice (Daniels et al., PNAS 2005, Lenard et al., Eur J Pharmacol, 2007). The aim of this study was to determine whether or not physical dependence, an important factor associated with opioid abuse in humans, developed after chronic treatment with MDAN-21.

**Methods:** Methods: Seven male Sprague-Dawley rats per treatment regimen. in the weight range of 260 - 280 g, received i.p. infusions, continuously for 4 days (Aceto et al., Eur J Pharmacol, 2000) with vehicle or escalating dose regimens of MDAN-21 or morphine sulfate. Then, MDAN-21 and morphine-treatment regimens were abruptly terminated and vehicle was substituted. A blind observer recorded body weight and withdrawal behavioral signs at 24-hr intervals for 4 days.

**Results:** Results: In the dose range 0.5 - 4 mg/kg/24 hr, the MDAN-21 treated rats and vehicle controls showed no statistically significant withdrawal behavior or body weight loss typically observed in the morphine controls. An equipotent antinociception dose regimen of MDAN-21 and morphine control was employed.

**Conclusions:** Conclusions: Given that the results of this study provide evidence that MDAN-21 has less physical dependence capacity than morphine, it may be useful in the pharmacotherapy of pain and opioid abuse.

**Support:** Supported by NIDA 7-8859 and DA15091.

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### THE RELATION BETWEEN ILLICIT DRUG USE IN METHADONE MAINTENANCE TREATMENT PATIENTS, PSYCHOPATHIC ASPECTS AND SENSE OF COHERENCE.

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**Aims:** to evaluate the relation between different facets of psychopathy, sense of coherence (SOC) and their relation to drug abuse among former heroin addicts currently in MMT.

**Methods:** Between September 2003 and October 2007, 66 non selective current MMT patients were studied. SOC questionnaire was used to measure the strength and coping skills of each individual, and divide them into Low-SOC (scored<145) and High-SOC (scored $\geq$ 145). The PCL-R instrument was used by patient therapist to assess psychopathic facets, creating factor 1 score (interpersonal/affective), factor 2 score (impulsive lifestyle/antisocial Behavior) and total score (factor 1+2). Observed randomized urines for opiates, cocaine, benzodiazepines, cannabis and amphetamines at the month prior to SOC questionnaire were taken, and drug abuse defined if at least one of the tests was positive.

**Results:** Low-SOC group (n=42) compared with High-SOC (n=24) group had higher factor 1 score (7.5+ 3.9 vs. 4.5+3.1, ANOVA  $F=10.1$ ,  $p=0.002$ ) and factor 2 score (11.8+ 3.61 vs. 7.8+4.24;  $F=16.8$ ,  $p<0.0005$ ). Patients who abused (n=35) as compared to those who did not abuse any drug (n=31) had higher factor 1 (4.6+ 2.9 vs. 8.5+ 3.8;  $F=21.7$ ,  $p<0.0005$ ), factor 2 (8.4+ 4.1 vs. 12.5+ 3.4;  $F=19.7$ ,  $p<0.0005$ ) and the total factor 1+2 score (14.8+ 6.9 vs. 23.7+ 6.9;  $F=27.6$ ,  $p<0.0005$ ). Patients with High-SOC and no drug abuse (n=18) had the lowest factor 2 score (7+ 3.85) following by High-SOC & drug abusers (n=6, 10+ 4.93), Low-SOC & not using (n=17, 9.82+4) and the highest factor 2 was among 25 patients with Low-SOC & drug abusers (13.12+ 2.65,  $F=10.3$ ,  $p<0.0005$ ). Factor 2 had negative linear correlation with SOC ( $R=-0.325$ ,  $p=0.008$ ) and with total factor 1+2 score ( $R=-0.297$ ,  $p=0.01$ ).

**Conclusions:** Patients in MMT who are characterized with strong psychopathic facets and weak SOC are less likely to stop drug abuse, especially those who had more antisocial and impulsive lifestyle behavior. Special interventions are needed to help this group of patients.

**Support:** The Adelson family foundation

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### INTRAVENOUS SELF-ADMINISTRATION OF ETONITAZENE ALONE AND COMBINED WITH COCAINE IN RHESUS MONKEYS: COMPARISON WITH HEROIN AND ANTAGONISM BY NALTREXONE AND NALOXONAZINE.

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**Aims:** In humans,  $\mu$  opioid-cocaine combinations (speedballs) have been reported to heighten pleasurable effects and result in greater abuse potential compared to either drug individually. Emerging evidence in animals suggests that the ability of  $\mu$  opioids to enhance the reinforcing effect of cocaine might be independent of their  $\mu$  agonist intrinsic efficacy even though  $\mu$  agonist efficacy appears to be a determinant in the reinforcing effects of  $\mu$  opioids. This study examined the relationship between agonist efficacy, self-administration and the enhancement of cocaine self-administration using the high-efficacy  $\mu$  agonist etonitazene.

**Methods:** Rhesus monkeys self-administered cocaine, heroin, etonitazene, and opioid-cocaine combinations under a progressive-ratio schedule of IV drug injection.

**Results:** Unlike cocaine and heroin, etonitazene did not maintain consistent self-administration at any dose tested (0.001 - 1.0  $\mu$ g/kg/injection). However, combining etonitazene (0.1 - 1.0  $\mu$ g/kg/inj) with cocaine (0.01 and 0.03 mg/kg/inj) enhanced cocaine self-administration and this enhancement was attenuated by naltrexone. These effects are similar to those obtained by combining non-reinforcing doses of heroin and cocaine. Antagonism of etonitazene-cocaine and heroin-cocaine self-administration by naloxonazine was short-lasting and was not maintained after 24hrs (when naloxonazine's purported  $\mu_1$  subtype antagonist effects are thought to predominate).

**Conclusions:** The results suggest that high  $\mu$  agonist efficacy does not guarantee significant drug self-administration; that the ability of  $\mu$  agonists to enhance cocaine self-administration does not depend exclusively on reinforcing efficacy; and do not support a role for  $\mu_1$  receptor mechanisms in opioid enhancement of cocaine self-administration.

**Support:** DA11928 and RR00168

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### ACCEPTABILITY OF AN MI-BASED TELEPHONE INTERVENTION FOR SUBSTANCE ABUSING TRANSPLANT PATIENTS.

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**Aims:** Substance abuse is the primary indication for organ transplantation, with 6-months abstinence typically required prior to surgery. Unfortunately, due to high medical acuity, most of those denied transplant do not receive treatment. The goal of the Transplant and Addiction Project (TAP) was to develop and pilot an MI-based telephone intervention that would allow medically ill patients to be conveniently treated in their own homes. One outcome of this Stage 1 Behavioral Therapies Development grant was acceptability of this distance intervention.

**Methods:** A 12-session treatment manual was developed and piloted on 20 transplant "rejects". We examined treatment retention, patient satisfaction, and helping alliance scores to determine acceptability of the intervention to both patients and their therapists.

**Results:** Participants were middle-aged (46.7/10.8) men (70.0%) of diverse ethnic background: 65% White, 20% Black, 10% Asian, and 40% Hispanic. Most were seeking a liver (75.0%), the remainder a kidney (25.0%). Of 20 participants randomized to the TAP intervention, 55% completed all 12 sessions (M=8.7(4.5); of the 9 non-completers, 1 died during treatment and 1 withdrew prior to starting treatment. Haq-II scores at discharge indicate that both patients (M=97.9, SD=19.7) and therapists (M=106.7, SD=6.7) forged a strong working alliance despite never meeting in person. In addition, participants rated the intervention highly on a satisfaction questionnaire (M for all items=4.5/5, SD=.5). Mean scores on a few items were: "Counselors were caring and non-judgmental" (M=4.8, SD=.4); "The intervention helped me deal with my alcohol and drug use" (M=4.8, SD=.5); "The program motivated me to stay sober" (M=4.8, SD=.9); and "Telephone counseling was convenient" (M=4.8, SD=.5).

**Conclusions:** Results suggest that telephone therapy for addiction problems is an acceptable alternative to traditional counseling. This type of intervention is widely exportable and may be most helpful for patients who are too ill to attend traditional substance abuse treatment.

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### INCREASED NEURAL RESPONSE TO LIDOCAINE RELATIVE TO PROCAINE IN HEALTHY SUBJECTS.

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**Aims:** Recent studies suggest that some of cocaine's central nervous system (CNS) effects may be mediated through its sodium channel inhibiting local anesthetic properties. Due to an absence of affinity at the DAT, the local anesthetic lidocaine may offer the potential to assess sodium channel activity in vivo in humans. To assess the utility of lidocaine as a CNS probe, we used single photon emission computed tomography (SPECT) to provide a net measure of lidocaine's effect upon CNS perfusion (regional cerebral blood flow, or rCBF). The response to lidocaine (0.5 mg/kg) was compared to procaine (0.5 mg/kg and 1.0 mg/kg), a local anesthetic with partial affinity for the DAT, and saline.

**Methods:** Intravenous infusions were administered, double-blind and pseudo-randomized, to nine healthy female controls over a ten-day period with at least two days between each scan. Lidocaine and procaine infusions were compared to saline ( $p < 0.005$ , cluster threshold 100) and differences between lidocaine and saline were compared to those between procaine and saline. rCBF was determined with SPM2.

**Results:** Increased rCBF was observed following lidocaine, relative to saline, in the striatum, insula, thalamus, pons, and posterior cingulate. Decreased rCBF was observed in the posterior cingulate. In general, changes in rCBF were more marked following lidocaine relative to either dose of procaine, particularly in the anterior insula and posterior cingulate (compared to procaine 0.5 mg/kg) and striatum (compared to procaine 1.0 mg/kg). Mood and sensory changes following lidocaine were limited and significantly less than those induced by either dose of procaine. There were no significant changes in blood pressure or heart rate following either medication.

**Conclusions:** Lidocaine (0.5 mg/kg) induces marked neural changes in healthy controls with minimal sensory, affective, and autonomic effects. Lidocaine can safely be used to assess sodium channel function in persons with cocaine addiction.

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### THE RISK OF DEVELOPING A DEPENDENCE SYNDROME IN RECENT ONSET USERS OF ANALGESIC COMPOUNDS.

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**Aims:** The National Survey on Drug Use and Health (NSDUH) indicated that there was a significant increase in lifetime extra-medical use of analgesic drugs among young adults from 2002-2004. This is inconsistent with trends for lifetime use of other illicit drugs which have remained stable. While initiation has not changed significantly from 2002-2004, the number of young adults that have become dependent increased significantly. In this study, we seek to estimate the risk of developing a dependence syndrome within 24 months after onset of extra-medical analgesic drug use and to determine if there is a male-female difference in these estimates.

**Methods:** Data are from a nationally representative sample of 111,184 participants in the 2005 and 2006 NSDUH, with confidential computer-based self-interviewing. Analyses included formal estimation of cumulative incidence and male-female variation in risk (with sample weighting; Taylor series variance estimation).

**Results:** Based on the experiences of 2,801 recent onset users of analgesic drugs, an estimated 3.6% developed a dependence syndrome within 24 months after onset of extra-medical analgesic drug use (95% CI= 2.8%, 4.5%). Female users were 1.9 times more likely to develop a dependence syndrome ( $p=0.038$ ). The strength of the association was maintained even after adjusting for age, income, and race (adjusted relative risk=2.1;  $p=0.007$ ). People aged 12-15 were at highest risk compared to people aged 18-20 (adjusted relative risk=2.7;  $p=0.004$ ).

**Conclusions:** Our estimates indicate that females have a significantly higher risk of developing a dependence syndrome. Further studies are required to determine how and why this male-female difference exists. In addition, our finding of an increased risk for adolescents also warrants giving attention to understanding their distinct path to dependence.

**Support:** NIDA award K05DA015799 & T32DA021129.

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### STIGMA ATTACHED TO DRUG DEPENDENCE AND DEPRESSION: PERCEPTIONS OF FUTURE HEALTH PROFESSIONALS.

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**Aims:** Stigma continues to block effective early outreach and intervention for mental health and behavior problems, including nicotine dependence. Stigma-related feelings held by future health professionals may shape their propensities to ask patients or clients about issues of drug dependence. In the current research, we compare and contrast future physicians and social workers surveyed to assess these stigma-related feelings toward drug dependence, with depression as comparison condition.

**Methods:** The study populations were defined by required class rosters for two recent cohorts of MD students (N=102) and MSW students (N=120) at a large midwestern university. For taking an anonymous classroom survey, all students received a fixed value online gift certificate (\$10), and drew at random a variable reinforcer certificate (\$12-\$35) to encourage completion of a linked but anonymous online survey including the Medical Condition Regard Scale (MCRS) to assess stigma feelings, with >90% survey completion. A GLM/GEE analysis was used for between-group comparisons.

**Results:** MCRS-rated stigma feelings were most negative as students contemplated treatment of patients/clients with drug dependence, less so for patients/clients with depression ( $p < 0.05$ ), even with covariate adjustment for student age and sex, both of which helped predict MCRS score ( $p < 0.05$ ). Nonetheless, MD and MSW students did not differ in these MCRS scores – i.e., product-term for type of program and stigma levels had  $p > 0.05$ .

**Conclusions:** Awareness and educational interventions are needed to mitigate stigma among future health professionals especially towards nicotine and alcohol dependence.

**Support:** NIDA awards K05DA015799, T32DA021129, and Michigan State University VPRGS research funds.

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### RISK-TAKING PROPENSITY AS A PREDICTOR OF INDUCTION ONTO NALTREXONE TREATMENT FOR OPIOID DEPENDENCE.

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**Aims:** Heroin addiction is a chronic relapsing disorder that has devastating social, medical, and economic consequences. Naltrexone is an opioid antagonist that blocks opioid effects and could be an effective medication for the treatment of opiate dependence. However, its clinical utility has been limited partly because of poor adherence and acceptability. Given the importance of compliance to naltrexone treatment for opiate dependence, the goal of the current study was to examine predictors involved in successful induction onto naltrexone treatment. **Methods:** In a sample of 56 individuals entering treatment for opiate dependence, we examined the relationship between naltrexone induction groups (i.e., induced- vs. not-induced onto naltrexone) and risk-taking propensity, as indexed by riskiness on the Balloon Analogue Risk Task (BART). **Results:** Of the 56 participants, 40 were successfully inducted onto naltrexone. BART score was predictive of induction onto naltrexone treatment, above and beyond injection drug use and cocaine-positive urine samples. Specifically, after adjusting for the covariates, each five point increase in BART score was associated with 28% decrease in the odds of achieving the maintenance dose (AOR=0.72, 95% CI: 0.52-0.99,  $p = .045$ ). **Conclusions:** The results may suggest implications for better understanding factors that underlie successful induction onto naltrexone, which could guide the development or modification of naltrexone treatment adherence for opiate dependence.

**Support:** This research was supported by NIDA grants R01 DA019386, R01 DA019497 and T32 DA07209.

**Conclusions:** The results may suggest implications for better understanding factors that underlie successful induction onto naltrexone, which could guide the development or modification of naltrexone treatment adherence for opiate dependence.

**Support:** This research was supported by NIDA grants R01 DA019386, R01 DA019497 and T32 DA07209.

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### SUBSTANCE USE OF FRENCH UNIVERSITY STUDENTS AT EXAM PERIODS: A CROSS-SECTIONAL SURVEY IN BORDEAUX.

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**Aims:** Little is known about French students' habits regarding medication and substance use. Moreover, no study has addressed exam periods.

The objective of this cross-sectional survey among French University Students was to assess the prevalence of medication and substance use and motivation for use, especially during exam periods.

**Methods:** A representative sample of undergraduate students was randomly selected in April 2007. Substance use during the year was assessed by a self-questionnaire including screening tools for alcohol (CAGE) and cannabis (CAST).

**Results:** Response rate was 99.0%. Subjects reported good quality of life, except for stress before exams (62.9%). Prevalence of medication use was low, with significant elevations during exam periods motivated by search for relaxation, sleep and intellectual performance. Prevalence of use at least once during the year was 38.2% for tobacco, 74.8% for alcohol and 26.0% for cannabis. Among them, 12.8% for alcohol and 24.0% for cannabis were detected as potential problematic users. Other illegal substance use (6.9%) was occasional. During exam periods, 48.3% of alcohol users reduced their drinking, and were significantly more often regular drinkers. 50.7% reported no variation, and were significantly more often occasional drinkers. 58.0% of cannabis users reported a reduction, and 38.1% no variation. 65.4% of regular tobacco users increased smoking.

**Conclusions:** Prevalence of medication use by students was low, but increased during exam periods. Prevalence of tobacco, alcohol and cannabis use were comparable to available studies. A large majority seemed able to control their use during exam periods, suggesting no addictive behavior, except for tobacco.

**Support:** UB2, INSERM IFR 99, ISPED, UB4

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### THE EFFECTS OF MDMA PREEXPOSURE ON MDMA-INDUCED TASTE AVERSIONS.

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**Aims:** Given the popularity of MDMA as a recreational drug, the present study used the conditioned taste aversion (CTA) preparation to assess how prior MDMA experience may impact the drug's aversive properties, and subsequent abuse potential.

**Methods:** Subjects were adult male Sprague-Dawley rats ( $n=36$  for Experiment 1;  $n=33$  for Experiment 2). During Experiment 1, a dose-response analysis of MDMA-induced CTAs was conducted using three doses of MDMA (1.0, 1.8, 3.2mg/kg) and vehicle, each paired with a novel saccharin solution. During Experiment 2, the effects of MDMA preexposure (1.8mg/kg; 5 spaced administrations) on MDMA (1.8mg/kg)-induced CTAs was assessed. The MDMA dose was chosen based on Experiment 1. Vehicle controls were provided for preexposure and conditioning phases.

**Results:** In Experiment 1, a  $4 \times 4$  ANOVA revealed significant main effects of Conditioning Treatment and Trial, as well as a significant Group  $\times$  Trial interaction ( $p's < 0.001$ ). HSD post-hocs revealed significant between-group differences in saccharin consumption on Trials 2-5; MDMA-induced CTAs were dose-dependent. In Experiment 2, a  $2 \times 2 \times 5$  ANOVA revealed significant main effects of Preexposure and Conditioning, as well as significant interactions of Trial  $\times$  Conditioning and Trial  $\times$  Preexposure  $\times$  Conditioning ( $p's < 0.05$ ). HSD post-hocs revealed significant between-group differences in saccharin consumption on Trials 2-5. Subjects preexposed and conditioned with MDMA consumed significantly more saccharin than vehicle preexposed subjects conditioned with MDMA on Trials 3 and 5.

**Conclusions:** In the present study, MDMA preexposure was found to attenuate MDMA-induced CTAs in rats. Results are interpreted to reflect pharmacological tolerance to the aversive properties of MDMA. Prior MDMA history may weaken the aversive effects of the drug upon subsequent administrations, thus increasing its abuse potential.

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### MENSTRUAL PHASE DIFFERENCES IN NICOTINE RESPONSE AFTER ACUTE SMOKING ABSTINENCE.

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**Aims:** Although mixed, both animal and clinical literature suggest estrogen may be associated with enhancing dopamine functioning in reward areas of the brain. We hypothesized that nicotine response would vary by menstrual phase after acute smoking abstinence, such that it would be more favorable in the follicular (F) phase as compared to the luteal (L) phase.

**Methods:** Participants ( $n=20$ ), ages of 18-40, with regular menstrual cycles who smoked five or more cigarettes per day and were not taking any exogenous hormones were recruited to participate in this within subject laboratory study. Participants completed two six-day testing sessions during the F and L phases. The first two days were smoking ad libitum followed by four days of biochemical verified abstinence. On the fourth day the participants completed a four-hour nicotine administration session. The Immediate Memory Task (IMT) was completed before and after nicotine administration (via nicotine nasal spray). Two measures of attention were computed using the IMT results: A' (the ability to discriminate between target and error stimuli; range 0.0-1.0, where 1.0 is perfect discrimination) and B''d (willingness to endorse an item as correct; range -1.0 to +1.0, where -1 is liberal bias and +1 is conservative bias). Paired t-tests were conducted to assess differences in absolute and change scores for A' and B''d by menstrual phase.

**Results:** Participants were  $29.6 \pm 6.9$  years of age and smoked  $14.0 \pm 5.4$  cigarettes per day. In the F phase participants became significantly more liberal in their willingness to endorse an item as correct after nicotine exposure, whereas in the L phase they became more conservative ( $-0.2 \pm 0.4$  vs.  $0.1 \pm 0.4$ ,  $p=0.02$ , respectively). There were no other statistically significant differences in measures of attention by menstrual phase.

**Conclusions:** The results of this preliminary analysis suggest that there may be menstrual phase differences in nicotine response after acute smoking abstinence. A larger study is currently underway to confirm these results.

**Support:** NIDA 5 R01-DA08075

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### HIV RISK BEHAVIORS AMONG SUBSTANCE-DEPENDENT NON-GAY IDENTIFYING MEN AND WOMEN WITH SAME-GENDER SEX EXPERIENCES.

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**Aims:** A new group at risk for HIV is men who identify as heterosexual but have sex with men (non-gay identifying men who have sex with men (NGI-MSM)). Previous studies have shown that drug use is common in this group, yet no research has assessed this group's or non-gay identifying women who have sex with women's (NGI-WSW) HIV risk within a substance dependent sample. We hypothesize that NGI-MSM will have increased HIV risk compared to heterosexuals; we do not expect such differences among NGI-WSW.

**Methods:** Data were obtained from the Addiction Health Evaluation And Disease management (AHEAD) study, a randomized study to assess a chronic disease management program for substance dependence. Subjects were recruited primarily from a detoxification unit. Information on sexual orientation/HIV risk behaviors were collected using audio-computer assisted self-interviewing (n=459). The outcomes were sex trade, condom use, knowledge of partners' HIV status, and needle sharing. A subject was categorized as NGI if they identified as heterosexual and reported same-gender sex in the past 90 days. However, we did not know the gender of sex partners with whom subjects engaged in sex trade or did not use condoms. All analyses were stratified by gender.

**Results:** 63% of women (79/125) and 21% of men (69/334) were categorized as NGI-WSW/MSM, respectively. Compared to heterosexuals, more NGI-WSW reported trading drugs/money to obtain sex (25.3% vs. 3.3%,  $p<0.0001$ ) while more NGI-MSM reported trading sex to obtain drugs/money (56.5% vs. 13.0%,  $p<0.0001$ ). NGI-WSW/MSM were similar to heterosexuals in other HIV risk behaviors.

**Conclusions:** Sex trade for money or drugs may explain the unexpectedly high prevalence of NGI-WSW/MSM among people with substance dependence. HIV prevention that targets sex trade may be especially important for NGI people with same-gender sex experiences.

**Support:** NIAAA/NIDA grants AA010870/DA010019.

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### ENDOCANNABINOID ALTERATIONS IN THE HIPPOCAMPUS AND NUCLEUS ACCUMBENS FOLLOWING CHRONIC COCAINE TREATMENT, DURING WITHDRAWAL AND FOLLOWING COCAINE CHALLENGE.

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**Aims:** Cocaine is a potent and addictive psychostimulant that alters dopamine and glutamate neurotransmission in the brain. One function of endocannabinoids (eCB), such as N-arachidonyl ethanolamine (anandamide, AEA) and 2-arachidonoylglycerol (2-AG), is as a retrograde messenger, modulating transmitter release via the presynaptic cannabinoid (CB1R) receptor. We hypothesized that AEA and 2-AG are altered, in a region-specific manner, following acute and chronic passive cocaine administration; and during cocaine withdrawal and subsequent challenge.

**Methods:** Male C57Bl/6 mice (15/gp) received 15 mg/kg ip cocaine for 10 days, then underwent 7 days of withdrawal followed by an injection of cocaine 1 day later. Brains were collected at Day 1 (Acute), Day 10 (Chronic), Day 17 (Withdrawal), and Day 18 (Challenge). Five regions were dissected: nucleus accumbens (NAc), prefrontal/orbitofrontal cortex (PFC), hippocampus, amygdala and motor cortex. AEA and 2-AG contents were quantified by isotope dilution, LC/MS and normalized to tissue weight.

**Results:** After 10 days of cocaine, 2-AG was suppressed vs saline control in the NAc ( $8032\pm603$  vs  $9841\pm490$  pMol/g [mean $\pm$ SEM],  $P=0.038$ ) while AEA was robustly decreased in the hippocampus ( $6.3\pm0.44$  vs  $8.3\pm0.54$  pMol/g,  $P=0.012$ ). Further, AEA in the hippocampus decreased over the duration of the study in both cocaine and saline groups (Treatment effect  $P=0.033$ , Phase effect  $P<0.0001$ , 2-way ANOVA). No changes in AEA or 2-AG were found in the amygdala or PFC.

**Conclusions:** Rather than a global shift, these data suggest that alterations in eCB content represent region- and ligand-specific changes in the mesocorticolimbic network. The suppression of AEA in the hippocampus and 2-AG in the NAc possibly suggest aberrant negative feedback, which would normally reduce the high transmitter release into these regions during cocaine receipt. Understanding the molecular bases of these changes in the eCB system could aid in the development of targeted pharmacotherapy for cocaine dependence.

**Support:** NIH/NIDA R21 DA022439 and F30 DA19754.

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### ESTROUS CYCLE EFFECTS ON PHYSIOLOGICAL RESPONSES TO PAIN IN FORMALIN- AND CARRAGEENAN-INDUCED INFLAMMATION.

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**Aims:** The aim of this study was to determine whether endogenous hormonal fluctuations during the estrous cycle of the Sprague-Dawley rat affect behavioral inflammatory-mediated intracellular mechanisms.

**Methods:** Methods: To this end, one of two types of inflammatory stimuli were administered. Intact eight week old intact Sprague-Dawley female rats were intraperitoneally injected with either 5% formalin (N=55) or 1% carrageenan (N=52). Trunk blood was collected from the formalin and carrageenan treated rats 1 hour and 5 hours post injection, respectively. Serum levels of corticosterone, an important mediator in inflammatory responses, were examined using radioimmunoassay kits.

**Results:** Results: The stage of the estrous cycle affected physiological responses to pain in both the formalin and the carrageenan studies. After formalin administration, females in estrus had significantly lower plasma corticosterone concentrations than females in diestrus [ $F(1, 55) = 1.72$ ,  $p<0.01$ ]. After carrageenan administration, females in proestrus had significantly lower corticosterone serum levels when compared to all other groups [ $F(1, 52) = 4.34$ ,  $p<0.01$ ].

**Conclusions:** Discussion and Conclusion: Taken together, our results suggest that fluctuation during the female endocrinological cycle effect physiological responses associated with inflammation.

**Support:** Supported by: SCORE 506-GM60654, MBRS-RISE GM60665, DA00325 and SNRP NS41073.

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### PROGESTERONE METABOLITE ALLOPREGNANOLONE ATTENUATES THE ESCALATION OF COCAINE-SEEKING BEHAVIOR IN FEMALE RATS.

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**Aims:** The purpose of the present study was to examine the effects of ALLO on the escalation of cocaine self-administration in female rats, and to compare results to previously tested groups that were treated with PROG or vehicle (VEH).

**Methods:** Rats were implanted with iv catheters, administered VEH, PROG (0.5 mg/kg), or ALLO (15 mg/kg), and trained to lever press for 0.4 mg/kg cocaine infusions under an FR 1 schedule during 2 h (short access, ShA) sessions. Once cocaine intake stabilized, the session length was extended to 6 h (long access, LgA) for 21 days. Following LgA, responses and infusions under the ShA condition were reassessed for the 3 groups.

**Results:** Similar to the results with PROG, ALLO-treated rats failed to increase cocaine self-administration during LgA, while VEH treated rats significantly increased cocaine self-administration across the 21 days. A comparison of cocaine infusions earned during LgA indicated that ALLO treated rats earned the fewest number of infusions compared to the VEH and Prog groups indicating that ALLO was more effective in decreasing cocaine self-administration than PROG at the doses tested. The ShA (FR 1) cocaine infusions were significantly higher after LgA than before in VEH-treated rats only; rats treated with PROG or ALLO did not show a post LgA increase in ShA cocaine intake.

**Conclusions:** These findings suggest that PROG and its metabolite, ALLO, show potential for attenuating binge-like patterns of cocaine intake, and they may serve as novel therapeutic agents in drug abuse treatment.

**Support:** Previous research indicates that progesterone (PROG) and its metabolite allopregnanolone (ALLO) decrease the reinstatement of cocaine-seeking behavior in female rats.

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### DISPELLING THE MYTH OF SMART DRUGS: CANNABIS USE PROBLEMS AND NONMEDICAL USE OF PRESCRIPTION STIMULANTS FOR STUDYING.

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**Aims:** Prescription stimulants are used nonmedically by college students ostensibly as "study aids", and a strong association has been documented cross-sectionally between nonmedical prescription stimulant use (NPS) and cannabis use. This study used four years of prospective data to test the following hypotheses: 1) Decreases in academic performance precede cannabis use problems and chronically skipping classes; and, 2) NPS for study purposes occurs subsequent to decreases in academic performance.

**Methods:** Undergraduates ( $N = 948$ ) attending a large public university in the U.S were interviewed annually for NPS, DSM-IV Cannabis Use Disorder, and frequency of skipping class. Semester grade point average (GPA) was obtained from administrative records. Growth curve modeling estimated the associations between a 6-level cannabis use variable that included abuse/dependence, GPA, percentage of classes skipped, and NPS for studying.

**Results:** Cannabis use problems were positively associated with skipping class ( $\beta = 0.020$ ;  $p < 0.001$ ), which in turn was related to declining GPA ( $\beta = -1.8$ ;  $p < 0.001$ ), which was then related to NPS by senior year for study purposes ( $\beta = -4.9$ ;  $p < 0.001$ ), after controlling for ethnicity, sex, family income, high school GPA, DSM-IV alcohol use problems, and ADHD status. Models with alternate pathways from cannabis use problems to NPS use did not fit the data as well.

**Conclusions:** There is a prospective relationship between the development of cannabis use problems and NPS. Results suggest that NPS for study purposes is not benign, but rather should be considered a compensatory behavior for decreased academic performance and chronic absenteeism in college students. Implications for prevention and early intervention are discussed.

**Support:** NIDA R014845, A. Arria, PI

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### A GLUTAMATERGIC ROLE IN WITHDRAWAL FROM BENZODIAZEPINES AS DETECTED VIA DRUG DISCRIMINATION ANALYSIS.

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**Aims:** Compensatory changes in glutamatergic neurotransmission as assessed by studies of seizure activity have been suggested to account for at least some of the WD symptoms associated with discontinuation of chronic BZ treatment. We used DD to assess changes in glutamatergic activity during BZ WD.

**Methods:** Male, Long-Evans rats ( $n=10$ ) were trained to discriminate 1.0 mg/kg i.p. diazepam (DZP). Following acquisition, rats were tested with either DZP (0.032-3.2 mg/kg) or MK801, an NMDA receptor antagonist (0.01-0.18 mg/kg), in a cumulative-dosing procedure across 3 consecutive days. Physical dependence to DZP was then induced by dosing rats every 12 ( $\pm 1$ ) hrs for 7 days with 20 mg/kg DZP. Rats again were tested for generalization to DZP or MK801 beginning 12 hours after the final dose on WD on days 1-5, 8, and 10.

**Results:** Predependence dose-response curves for DZP generalization were relatively stable with most rats showing full generalization ( $>80\%$  DZP-lever responding) at 0.32 mg/kg for at least 2/3 of the tests. Following termination of chronic DZP, all rats showed signs of BZ WD. Dose-response curves for DZP on WD1-3 were shifted to the right such that more DZP was needed to produce full DZP generalization. By WD4, the DZP generalization gradient was back to baseline. Rate-decreasing effects of high DZP doses were reduced during WD. Pre-dependence dose response curves for MK801 also were relatively stable with most rats showing no DZP-like responding (though one rat did show full generalization). During WD tests, 3 of 4 rats showed at least partial generalization ( $>20\%$  DZP lever responding) on at least 1 WD day. MK801 also produced less of a decrease in rates of responding during WD particularly on WD4-5 compared to baseline.

**Conclusions:** Changes in glutamatergic activity during withdrawal from BZ thus appear not only to be a component of BZ WD but to be detectable by DD analysis.

**Support:** Supported by NIDA grant R01 04133.

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### HOMER2 EXPRESSION BIDIRECTIONALLY REGULATES PFC GLUTAMATE LEVELS: RELATION TO COCAINE REWARD.

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**Aims:** Withdrawal from repeated cocaine up-regulates Homer2b expression in the prefrontal cortex (PFC). Thus, the present study sought to determine the role of PFC Homer2b in cocaine addiction-related behaviors and the regulation of PFC glutamate transmission.

**Methods:** Adult male C57BL/6J mice received intra-PFC infusions of adeno-associated viral vectors (AAVs) carrying either cDNA for, or shRNA against, Homer2b cDNA. Following a behavioral test battery, animals were tested for cocaine-induced changes in psychomotor activation and reward in a CPP paradigm (4x15 mg/kg). PFC basal glutamate content, Group1 mGluR function and the ability of acute and repeated (7 X 15 mg/kg) cocaine injections to alter PFC glutamate levels were also assessed.

**Results:** Homer2b shRNA elevated spontaneous locomotor activity, but cDNA did not affect spontaneous behaviors. Homer2b cDNA potentiated cocaine CPP, but not locomotor sensitization. shRNA reduced basal glutamate levels when compared to controls, while cDNA increased moderately glutamate content. Repeated cocaine sensitized glutamate release in controls. Interestingly, shRNA facilitated, while cDNA abolished, the glutamate response to acute cocaine and neither AAV group exhibited glutamate sensitization upon repeated cocaine treatment. Neither cDNA nor shRNA altered glutamate release elicited by the Group1 mGluR agonist DHPG; however, shRNA potentiated depolarization-induced glutamate release.

**Conclusions:** Cocaine-induced increases in PFC Homer2b expression is sufficient, but not necessary, for cocaine reward, independent of changes spontaneous behaviors or cocaine-induced locomotion. Moreover, Homer2b bidirectionally regulates PFC basal and acute cocaine-stimulated glutamate release and perturbations in PFC Homer2b expression can impact the excitability of PFC glutamate terminals, as well as the capacity of repeated cocaine to induce glutamate plasticity within this region.

**Support:** Supported by NARSAD and NIDA grant DA024038 (KKS).

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### PROSPECTIVE EXAMINATION OF THE ASSOCIATION OF STIMULANT MEDICATION HISTORY AND DRUG USE OUTCOMES IN ADHD YOUTH.

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**Aims:** To compare ADHD groups (with and without history of psycho-stimulant medication) on the extent and pattern of subsequent drug use involvement and substance use disorders during late adolescence and young adulthood.

**Methods:** We present self-reported drug use outcomes from assessment waves 4 - 6 of ADHD probands ( $N = 149$ ; ages 19 - 24) who varied as to the degree of exposure to psychostimulant medication as a child. Extent and pattern of several drug use outcomes will be compared between the ADHD-no medication, ADHD-childhood only medication, and ADHD-childhood and adolescent medication.

**Results:** No evidence was found to support the hypothesis that childhood treatment with stimulant medication, including the course of stimulant medication, is associated with any change in risk for adolescent or young adulthood drug use behaviors. This pattern of results applied to alcohol, nicotine and illicit drugs, and to presence/absence of substance use disorders.

**Conclusions:** Study results support the growing body of literature indicating that stimulant treatment does not create a significant risk for subsequent substance use disorders. Our study importantly extends this literature. Whereas extant data have come from clinic-derived samples, our study is based on a community-based sample of ADHD children, which may represent a greater proportion of ADHD youth than those seen in clinics.

**Support:** This study was supported by grants K02 DA015347 and R01 DA012995 from the National Institute on Drug Abuse.

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### PAIN ASSESSMENT IN PATIENTS ON OPIOID MAINTENANCE THERAPY.

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**Aims:** Chronic administration of opioids has been associated with hyperalgesia, partially explaining chronic pain problems in opioid maintenance therapy. Hypothesis : opioid maintained patients display a significant decrease of pain thresholds compared to matched control subject

**Methods:** A clinical study with a three arms design was used. Pain thresholds to a mechanical and an electrical stimuli were compared between treated patients with an opioid dependence (30 MET/30 BUP) and 30 control subjects. Psychopathological scales (ASI, HAD, SF36) were used. Mechanical and electrical tests, to assess changes in pain thresholds, have been carried out at Tmax (3h or 1h30) and T24h after treatment administration

**Results:** No difference between both treated groups was noticed regarding HAD, SF36 and ASI scores. In MET maintained patients, compared to control subjects (152+/-17g and 10.8+/-3.7 respectively), we observed at T3h and 24h a significant decrease in mechanical (132+/-26g,  $p=0.02$  and 109+/-23g,  $p<0.0001$ ) and electrical (6.4+/-3.7,  $p=0.0003$  and 6+/-4.3,  $p=0.0003$ ) pain thresholds but also a significant difference ( $p<0.0001$ ) between T3h and T24h only after a mechanical stimulus. In BUP maintained patients, compared to control subjects (154+/-29g and 8.9+/-2.1), we displayed at T24h a significant decrease in mechanical (133+/-17g,  $p=0.015$ ) and electrical (6.9+/-2.4,  $p=0.045$ ) pain thresholds but also a significant difference ( $p=0.039$ ) between T1h30 and T24h only after a mechanical stimulus. Pain thresholds were significantly decreased in MET group compared to BUP group, at T24h, both after a mechanical ( $p=0.003$ ) and an electrical ( $p=0.04$ ) stimulus. The prevalence of hyperalgesic patients were 3-fold higher ( $p=0.02$ ) in MET than BUP group

**Conclusions:** We demonstrate a significant decrease of pain thresholds in maintained patients, a particularly pain-sensitive population who need a great attention during potential painful cares

**Support:** PHRC CHU Clermont Fd

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### NEURAL CORRELATES OF IMPAIRED NUMBER PROCESSING IN YOUNG ADULTS WITH PRENATAL ALCOHOL EXPOSURE.

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**Aims:** Specific deficits in number processing are associated with prenatal alcohol exposure (PNAE). We hypothesized that these impairments would be associated with functional alterations in the networks subserving number processing.

**Methods:** Participants were 10 exposed (AE) and 9 non-exposed (NE) right-handed, African American young adults (18-20 yr) from the Detroit Prenatal Alcohol Exposure Cohort. Maternal alcohol and drug use were ascertained prospectively during pregnancy. The fMRI task consisted of an Exact Addition paradigm with a letter matching control condition.

**Results:** AE and NE performed well on the task (% correct: AE=91.2; NE=93.5;  $p>0.50$ ). AE showed significantly ( $p<0.05$ ) weaker activation of angular gyrus (AG, bilateral), left intraparietal and precentral sulci and left dorsolateral prefrontal cortex. Furthermore, AE showed less AG activation for addition compared with letter matching, suggesting less capacity to engage a network that was intact for letters in encoding the verbal representation of numbers. This observation led us to predict poorer performance in standardized achievement tests of arithmetic, compared with reading. This was confirmed by an analysis of covariance examining the Wechsler Individualized Achievement Test (WIAT) of arithmetic administered to the same individuals at 14 years of age. The effect of PNAE remained significant after controlling for WIAT reading ( $F(1, 275)=4.13$ ,  $p<0.05$ ). Conversely, the effect of PNAE on WIAT reading was no longer significant after controlling for WIAT math ( $F(1, 275)<1$ ).

**Conclusions:** These data provide a neural basis for the relative sparing of reading ability compared with arithmetic in PNAE. They further suggest that an intervention designed to improve semantic representation of numbers early in development may be warranted in PNAE.

**Support:** Support: DA021034, AA069666, AA09524, Joseph Young, Sr. Fund

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### PROGESTERONE MODULATION OF TRIAZOLAM EFFECTS IN HEALTHY WOMEN.

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**Aims:** Previous research suggests that the effects of sedative drugs among women may be enhanced during the luteal phase of the menstrual cycle. These ongoing studies build on previous research by examining whether sensitivity to the central effects of triazolam is enhanced by progesterone pre-treatment.

**Methods:** The first study examines the effects of triazolam, alone and in combination with progesterone, in healthy, premenopausal women. Participants complete cardiovascular measures, verbal reports of drug effect, and computer tasks designed to assess psychomotor and impulsive behavior during 9 sessions in the early follicular phase of their menstrual cycle and are administered progesterone (0, 100, 200 mg, po) and triazolam (0, .12, .25 mg/70 kg, po) alone and in combination under double-blind conditions. Drug effects are analyzed using repeated measures ANOVA with triazolam dose, progesterone dose and time as factors. A follow-up study examines whether the discriminative stimulus effects of triazolam are enhanced by progesterone pre-treatment. After triazolam discrimination has been established (training dose: .25 mg/70 kg triazolam), test doses (0, .06, .12, and .25) of triazolam are administered alone and in combination with oral progesterone (100 mg). Assessments are identical to those in the first study, except for the addition of the drug discrimination task in post-dose sessions.

**Results:** The results of the first study indicate that triazolam engenders prototypical sedative-like behavioral effects, with progesterone producing few measurable effects. In combination, progesterone enhances the magnitude of triazolam effects. Data collection for the second study, hypothesizing that progesterone will enhance sensitivity to the discriminative stimulus effects of triazolam, is ongoing.

**Conclusions:** These results suggest that benzodiazepine effects are sensitive to hormone modulation and acute drug effects in women may be influenced by variations in progesterone levels.

**Support:** DA-024127, RR-15592.

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### GENDER DIFFERENCES IN PRESCRIPTION OPIOID DEPENDENCE: A PILOT STUDY.

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**Aims:** Prescription opioid (PO) non-medical use is on the rise among both men and women (Blanco et al., 2007; Rawson et al., 2007). Recent data suggest that women are more likely than men to be prescribed a pain medication (McCabe et al., 2005) and are 23% times more likely than men to present at emergency rooms secondary to the non-medical use of prescription drugs (SAMHSA, 2007). Greater understanding of gender differences regarding PO use is needed to assist in the development of gender-specific interventions.

**Methods:** Participants were 24 outpatients (12 women, 12 men) dependent on POs. Participants completed a clinical interview and responded to standardized questions regarding their PO and other substance use.

**Results:** The most commonly used POs included Lortab® (50.0% men, 58.3% women) and OxyContin® (66.7% men, 41.7% women). Average age of first use was 23.3 (SD=9.8). The average latency between first use and problematic use was 7.8 years for men and 3.9 years for women. Men were significantly more likely than women to crush and snort POs (75.0% vs. 16.7%,  $p=.01$ ). Although not statistically significant, men reported higher rates of injecting POs, as well (41.7% vs. 16.7%). Over half of men (57.1%) and women (66.7%) reported chewing POs. Men were more likely than women to report using POs for pain (100.0% vs. 66.7%,  $p=.09$ ). Other common reasons included stress (45.5% men, 66.7% women), depression (45.5% men, 58.3% women), withdrawal symptoms (45.5% men, 50.0% women) and to get "high" (100.0 men, 66.7% women). Regarding triggers for use, significantly more women than men reported being triggered to use POs secondary to interpersonal stress ( $p=.04$ ) and negative emotions, such as guilt and shame ( $p=.09$ ). The majority of men (100.0%) and women (75.0%) reported using other substances (e.g., marijuana, alcohol) concurrently with POs.

**Conclusions:** A number of gender difference were revealed, particularly with regard to method of administration and triggers for use. These preliminary findings help identify gender differences in PO use and may have important clinical implications.

**Support:** K23 DA021228 (PI: Back)

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### EARLY METHYLPHENIDATE EXPOSURE ENHANCES COCAINE SELF-ADMINISTRATION BUT NOT COCAINE-INDUCED CONDITIONED PLACE PREFERENCE IN YOUNG ADULT RATS.

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**Aims:** Methylphenidate (MPH) treatment during the preweaning period enhances the reinforcing effects of morphine in adulthood. Similar studies using cocaine have yielded conflicting results depending on whether reward was assessed using the self-administration or condition place preference (CPP) paradigms. The goal of the present study was to examine the effects of early MPH exposure on cocaine-induced responding using both reward paradigms.

**Methods:** Rats were pretreated with MPH (0, 2, or 5 mg/kg) from PD 11 to PD 20 and then cocaine-induced CPP or cocaine self-administration was measured in young adulthood. A 10-day CPP procedure was used, which included one pre-conditioning day, eight conditioning days (consisting of alternating daily injections of saline or 0, 10 or 20 mg/kg cocaine), and one test day. After the initial CPP test, rats were given 8 days of extinction training followed by a test day. After this test day, rats were given a priming dose of cocaine (10 mg/kg) before reinstatement testing. For the self-administration experiment, an indwelling jugular catheter was implanted and rats were trained to press a lever for cocaine (0.25 or 0.75 mg/kg) on an FR1 schedule. Rats were gradually moved from an FR1 to an FR10 schedule and, after criterion was reached, rats were placed on a progressive ratio schedule for five days.

**Results:** Cocaine produced robust rewarding effects in both the CPP and self-administration experiments; however, early MPH exposure only affected reward on the self-administration paradigm. Specifically, MPH-exposed rats had a greater number of self-administered cocaine infusions than control rats. In contrast, early MPH exposure did not affect the acquisition, extinction or reinstatement of cocaine-induced CPP.

**Conclusions:** The present data, along with previous findings from our laboratory, suggest that early MPH exposure may enhance the vulnerability of young adults to both opioid and psychostimulant drugs.

**Support:** GM073842 to CAC

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### DOES DAY OF WEEK IMPACT PREVALENCE OF PRESCRIPTION DRUG ABUSE?

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**Aims:** Abuse and misuse of prescription drugs (APD) is a significant problem in the US. Understanding associated behavioral factors may help in treatment or education efforts. We evaluated APD temporal trends involving day of week to see if APD was affected by behaviors associated with weekends or weekdays using RADARS® System Poison Center (PC) data.

**Methods:** Spontaneous calls from the public and healthcare professionals are recorded by PC using a standardized, electronic data collection system. Intentional exposures for the following prescription drugs (PD) were analyzed: methadone, hydrocodone, oxycodone, morphine, fentanyl, buprenorphine and oxymorphone. Daily intentional exposure case count from 43 PC by day of the week for 2003 -2007. Additionally weekday (Monday-Friday) was compared to weekend (Saturday-Sunday). Statistical analysis was by ANOVA and Bartlett's test for inequality of population variances. APD cases were compared with volume of all PC to evaluate if total daily call volume impacts APD call volume.

**Results:** Over the study period mean and median case prevalence by day of week ranged from 77.8 to 79.8 per day and 83 to 86 per day, respectively. Mean percent of cases by day of week ranged from 14.03% to 14.39%, with slightly higher use on weekend days. There was no significant difference when evaluating prevalence of APD by day of week ( $p = 0.99$ ). There was no significant difference when evaluating weekend versus weekday ( $p > 0.05$ ). In contrast to APD cases, total cases for all substances managed by PCs (pharmaceutical and non-pharmaceutical) showed a consistent 7% decrease on weekend days.

**Conclusions:** Prevalence of APD appears to reflect a steady pattern consistent with a routine use as compared to periodic use.

The prevalence of misuse and abuse of prescription drugs as reported to RADARS® System Poison Center (PC) data was not impacted by day of the week or difference between weekday and weekend.

**Support:** This study was supported by a grant from the RADARS system.

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### EFFECTS OF 3,4-METHYLENEDIOXYMETHAMPHETAMINE ON ARGININE VASOPRESSIN IN HEALTHY VOLUNTEERS.

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**Aims:** Illicit MDMA use has been associated with hyponatremia, particularly in females. A previous study found that MDMA administration elevated plasma arginine vasopressin (AVP, antidiuretic hormone) levels in healthy volunteers. However, the study employed a lower dose than is commonly used by illicit users and only included males. We sought to measure AVP and serum sodium after a psychoactive dose of MDMA in both males and females.

**Methods:** Eight males and eight females, all healthy and MDMA-experienced, received 1.5 mg/kg oral MDMA alone and in combination with the alpha-1 adrenergic inverse agonist prazosin in a placebo-controlled, within-subjects randomized controlled trial. AVP and serum sodium were measured before and 1, 2, 3, 4, and 6 hours after MDMA. AVP Cmax were determined and analyzed using linear models.

**Results:** Despite having robust psychoactive effects, MDMA did not significantly affect AVP (Cmax was  $2.394 \pm 5.042$  (mean  $\pm$  95%CI) after MDMA vs.  $5.000 \pm 5.042$  after placebo,  $p = 0.468$ ) or serum sodium ( $140.38 \pm 0.917$  vs.  $139.50 \pm 0.917$  mmol/L at TMax for AVP for MDMA vs placebo,  $p = 0.182$ ). However, two male volunteers had brief large AVP elevations after MDMA (28.8 and 18.7 pg/mL at 1 hr post dose).

**Conclusions:** AVP elevations in illicit MDMA users may represent an idiosyncratic response to MDMA. Additional mechanisms, including excessive water intake, may contribute to hyponatremia in illicit MDMA users.

**Support:** DA 016776

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### FOOD RESTRICTION DIFFERENTIALLY MODIFIES THE BEHAVIORAL EFFECTS OF THE DOPAMINE RECEPTOR AGONIST QUINPIROLE IN RATS.

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**Aims:** Food restriction decreases sensitivity to some behavioral effects (e.g., yawning) of quinpirole, a direct-acting dopamine (DA) receptor agonist. This study used drug discrimination to further examine possible changes in DA systems that might be relevant to understanding how nutrition impacts the effects of drugs of abuse (e.g., cocaine) acting on DA systems. Most discrimination studies use food to maintain lever pressing; the current study established a discrimination with quinpirole in free-feeding rats responding under a schedule of shock avoidance so that diet could be systematically manipulated.

**Methods:** Six male Sprague Dawley rats discriminated .032 mg/kg quinpirole in sessions consisting of 1-4, 20-min cycles. Each cycle began with a 10-min timeout followed by illumination of a house light that signaled the delivery of a brief shock stimulus every 10-s; a response on the correct lever or the passage of 30-s turned off the house light, ended the trial, and initiated a 30-s timeout. The discrimination was first established with an acute dosing, single cycle procedure after which the conditions were changed to a cumulative dosing, multiple cycle procedure. Tests were conducted after rats satisfied the following criteria under multiple cycles: at least 80% of trials completed and the first response of each trial occurring on the correct lever for 4 consecutive or 5 out of 6 sessions.

**Results:** Under multiple cycles, responding was under adequate stimulus control for testing after an average of 18 training sessions. Saline and .0032 mg/kg quinpirole occasioned responding predominantly on the saline-associated lever, whereas larger doses of quinpirole (.01 and .032 mg/kg) increased responding on the quinpirole-associated lever. Food restriction (10 g/day for up to one week) that abolished quinpirole-induced yawning had little to no effect on the discriminative stimulus effects of quinpirole.

**Conclusions:** These results demonstrate that behavioral effects of DA receptor agonists are differentially modified by food restriction.

**Support:** CPF is supported by a Senior Scientist Award (DA17918).

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### ONTOGENY-DEPENDENT ROLES OF STRIATAL NNOS AND TYROSINE HYDROXYLASE IN THE DEVELOPMENT OF LONG-LASTING COCAINE-INDUCED SENSITIZATION IN MICE.

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**Aims:** Little is known about the long-term effects of adolescent cocaine exposure and the neural substrates involved in sensitization to cocaine in adolescence compared to adulthood. The aims of the present study were to investigate: a) the development of cocaine-induced sensitization from adolescence through adulthood, and b) the roles of the neuronal nitric oxide synthase (nNOS) gene and tyrosine hydroxylase (TH) in the development of sensitization in adolescence and adulthood.

**Methods:** Adolescent (postnatal day [PD]28) and adult (PD80-90) male wild type (WT) and nNOS knockout (KO) mice received saline or cocaine (20mg/kg; IP) for five days. Separate groups were challenged with cocaine (20mg/kg) 10, 30 or 90 days after discontinuation of drug injection, and locomotor activity was recorded. Changes in striatal nNOS- and TH-expression were determined by western blot and immunohistochemical analysis 1 and 10 days after cocaine administration had ceased.

**Results:** Adolescent WT and nNOS KO mice, and adult WT mice, developed long-lasting sensitization to cocaine, i.e. 3 months after repeated drug administration had ended. In contrast, adult nNOS KO mice were resistant to cocaine sensitization. Repeated cocaine administration resulted in a) a 96% increase in dorsal striatum (dST) nNOS-immunoreactive neurons in adult but not adolescent WT mice, b) overexpression of dST TH in adult but not adolescent WT mice and c) a decrease in dST TH expression in adult but not adolescent nNOS KO mice.

**Conclusions:** Results show that a) adolescent and adult WT mice developed exceptionally long-lasting sensitization to cocaine, b) the nNOS gene is necessary for the development of sensitization in adults but not in adolescents, c) induction of sensitization in adulthood, but not in adolescence, may depend on overexpression of dST nNOS and TH, d) different neural substrates appear to be involved in the development of cocaine sensitization in adolescence and adulthood.

**Support:** Supported by DA019107 (YI) and DA022847 (MB)

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### BRAIN MR SPECTROSCOPY IN THE FRONTAL WHITE MATTER OF PRENATALLY COCAINE-EXPOSED ADOLESCENTS.

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**Aims:** To quantify metabolites in frontal white matter (FWM) of prenatally cocaine-exposed (CE) and non-cocaine-exposed (NCE) adolescents using in vivo proton MRS.

**Methods:** A subsample of 31 boys (16 CE;15 NCE) ages 12-15 and 28 girls (10 CE;18 NCE) ages 15-17 in the Miami Prenatal Cocaine Study received whole-brain T1-weighted MRI and single-voxel proton spectroscopy of right (R) and left (L) FWM (3 Tesla; point-resolved sequence, TR/TE: 2s/30ms, voxel ~3.4 cc, acq time 8.4 min). T1-MRIs were segmented into cerebrospinal fluid (CSF) and parenchyma for metabolite quantitation. N-acetyl aspartate (NAA), total creatine (Cr), total choline (Cho), glutamate+glutamine (Glx) and myo-inositol (m-Ins) were quantified in institutional units with in-house software. Abnormal structural scans or poor quality spectra were excluded. Paired and unpaired t-tests were used with p<0.05 considered significant.

**Results:** Boys: There was a significant difference (R>L) for Glx and Glx/Cr in both CE and NCE and for Cho and Cho/Cr in CE. CE vs NCE had higher levels of m-Ins/Cr bilaterally. CE>NCE differences approached significance for RFWM m-Ins (p=0.09) and Glx/Cr (p=0.06). Girls: There was a significant R>L difference for Glx/Cr in NCE and near-significant R>L difference (p=0.076) for Glx in CE. CE vs. NCE had significantly higher RFWM Cho/Cr and LFWM m-Ins/Cr. CE>NCE differences were near-significant for RFWM Cho (p=0.06).

**Conclusions:** Preliminary results of this in vivo proton MRS single voxel study suggest that prenatal cocaine exposure may induce significant alterations in brain metabolites of frontal white matter, predominantly on the right, in developing adolescents and that alterations in specific metabolites may vary by gender. Future work correlating MRS findings with neuropsychological outcomes and comparing males and females at comparable ages in later adolescence should elucidate the clinical significance of these results.

**Support:** R21DA15906; R01DA006556; P50DA024584; M01RR16587

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### EFFECTS OF THE COMPETITIVE NMDA RECEPTOR ANTAGONIST LY235959 ON THE ANTINOCICEPTIVE RESPONSE TO ACUTE AND CHRONIC MORPHINE IN WT AND NR1 KD MICE.

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**Aims:** The present study determined whether the competitive NMDA receptor antagonist LY235959 would attenuate the development of tolerance to the antinociceptive effects of morphine in mice with a 90% decrease in NMDA expression (NR1 KD).

**Methods:** Initially, morphine dose-effect curves were obtained in NR1 KD mice and their wild-type littermates (NR1 WT) in a 56°C hotplate procedure using a cumulative dosing procedure in which increasing doses of morphine (0.32 – 32 mg/kg, s.c.) were administered every 30-min. Tolerance was then induced by administering increasing doses of morphine, based on individual ED50s, twice daily (10am and 8pm) for 12 days. Mice received LY235959 (1.0mg/kg, s.c.) or saline with each morphine injection. On day 14, morphine dose-effect curves were redetermined. Immediately after, naltrexone (1.0 mg/kg i.p.) was administered and mice were placed in pyrex beakers (4L) for 30 min to observe withdrawal jumping.

**Results:** The acute morphine ED50 was 2.6 mg/kg in NR1 WT and 10.3 mg/kg in NR1 KD mice, revealing approximately a 3-fold difference in potency between the genotypes. Following 12 days of chronic administration, the ED 50s in the NR1 WT and NR1 KD mice that received saline plus morphine were increased to 12.4 and 24.1 mg/kg, respectively. In mice that received LY235959 plus morphine, the ED50s remained approximately the same: 13.9 mg/kg in the NR1 WT mice and 31.9 mg/kg in the NR1 KD mice. Robust naltrexone induced jumping was observed in all groups.

**Conclusions:** Morphine was less potent in NR1 KD mice as compared to NR1 WT mice although both groups developed morphine tolerance to a similar degree. Chronic administration of an NMDA antagonist during the tolerance regimen did not attenuate the development of tolerance to morphine in either the NR1 KD or the NR1 WT mice. These data suggest that a chronic decrease in NMDA receptor activity does not prevent the development of morphine tolerance.

**Support:** NIH RO1-DA02749 and T32-DA007244

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### EFFECTS OF EXTENDED ACCESS AND WITHDRAWAL ON THE REINFORCING STRENGTH OF COCAINE USING A COCAINE VS. FOOD CONCURRENT-CHOICE PROCEDURE IN RHESUS MONKEYS.

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**Aims:** Drug withdrawal may increase the reinforcing strength of some classes of abused drugs. However, the effects of cocaine withdrawal on the reinforcing strength of cocaine have produced divergent results. This study examined effects of graded periods of cocaine access and withdrawal on the relative reinforcing strength of cocaine using a cocaine vs. food concurrent-choice procedure.

**Methods:** Cocaine (0 – 0.1 mg/kg/inj) and banana pellets were available under a concurrent-choice schedule during daily 2-hr sessions (n=4). Subsequently, extended access to cocaine was introduced via availability of 0.1 mg/kg/inj cocaine under a FR 10/ Time Out X schedule during 21hr sessions that followed daily choice sessions. The degree of access was manipulated by varying the time-out (30, 15, 7.5 min). Extended access with each TO was introduced for 1 week, followed by at least one week of withdrawal.

**Results:** Cocaine maintained a dose-dependent increase in cocaine choice. Cocaine intake increased as TO decreased, and peak intake was approximately 11 mg/kg/day. Neither extended cocaine access nor withdrawal altered cocaine choice.

**Conclusions:** Under these conditions, extended cocaine access and withdrawal failed to alter the relative reinforcing strength of cocaine.

**Support:** Research supported by P01-DA14528 from NIH/NIDA.



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**ETHNICITY AND RECENT-ONSET TOBACCO SMOKING: EPIDEMIOLOGICAL EVIDENCE, 2004-06.**

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**Aims:** Large-sample epidemiological studies of tobacco smoking routinely assess what has happened in the distant past (e.g., so-called 'lifetime prevalence' of tobacco dependence). Instead, our research group looks into the earliest stages of drug involvement in the recent past. In this study, we focus attention upon a very rapid transition from first tobacco smoking toward an acceleration in days of recent-onset smoking, with a hypothesis that ethnicity may signal variation in progressions to tobacco dependence once smoking starts.

**Methods:** Data for this study are from 2004-6 National Surveys on Drug Use and Health (NSDUH, n=167,000), designed to produce a nationally representative sample of community-dwelling U.S. citizens age 12+ years, of whom 2750 had started smoking tobacco within 24 months of the assessment date and were asked about the number of recent smoking days. Analysis involved a Poisson count regression model for complex sample design and sampling weights, with sex and age as covariates (STATA 9.2).

**Results:** Among these recent-onset smokers, non-Hispanic Whites, non-Hispanic Black/African Americans, Asians, and Native American/Alaskan Natives did not differ, but recent-onset smokers of Hispanic origin, and those of Pacific Islander background, reported robustly fewer recent days of smoking (Hispanic  $\beta = -0.2$ , 95% CI = -0.4, -0.04; Pacific Islanders  $\beta = -1.0$ , 95% CI = -1.7, -0.2).

**Conclusions:** Once tobacco smoking starts, prevention of tobacco dependence may require interpersonal and social transactions that constrain a mounting frequency of days of smoking. Micro-social process research of an ethnographic character may shed light on important interpersonal and social transactions that now slow progress toward tobacco dependence in our Hispanic and Pacific Island communities.

**Support:** NIDA awards, T32DA021129, K05DA015799, R01DA016558, MSUVPRGS funds

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**FIELD CLINICIAN REPORTS OF IMPLEMENTATION OF EVIDENCE-BASED PRACTICE.**

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**Aims:** The well-acknowledged communication gap between researchers and community-based substance abuse treatment programs has hindered practitioner adoption of empirically-derived addiction treatment technologies. This NIDA-funded program examines some of the issues related to knowledge exchange between researchers and community practitioners. Field clinicians were offered evidence-based training (based on Behavioral Couples Therapy [BCT]) in a training workshop. The practical issues and roadblocks of implementation of this training material into clinical practice are discussed in this poster.

**Methods:** Participants were assigned to one of three follow-up conditions; (1) enhanced Post-Training Support Center, (2) telephone support and (3) no additional support. The participants in the telephone support group received up to weekly telephone follow-up contact from expert BCT therapists for six months following training. During these telephone contacts, issues related to the individuals' attempts to implement the program offered in the training workshop were discussed and recorded.

**Results:** The participants reported a series of roadblocks to implementing BCT in their practices. These roadblocks included: changes in participants' enthusiasm over time, time to prepare, need to change clinical style from primarily process sessions to manual-based, needing more time per session to accomplish prescribed tasks, lack of supervision support, patient drop-out, and reimbursement issues.

**Conclusions:** The implications of this research may be important, as it offers a unique perspective on the issues of implementation tracked over the course of six months. Some of the issues were familiar, while concerns were only clearly revealed as a result of being able to be in contact with clinicians over an extended period of time. The findings may prove helpful in planning technology transfer outreach and research efforts.

**Support:** This project is supported by NIDA R01 DA018295.

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**SUBSTANCE USE, POSTTRAUMATIC STRESS DISORDER AND VIOLENT CRIME.**

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**Aims:** This paper aims to examine the relationship between substance use disorder (SUD), posttraumatic stress disorder (PTSD) and violent crime. SUD and PTSD have independently been associated with high rates of crime. It is possible that the combination of SUD symptoms (e.g., impulsivity, aggression and reduced inhibition) and PTSD symptoms (e.g., hypervigilance, irritability and anger) in individuals with this comorbidity may increase susceptibility to crime, in particular, violent crime. Very little research has been conducted to examine the validity of this claim.

**Methods:** Data was collected from 84 participants recruited to a randomised controlled trial of an integrated treatment for comorbid SUD and PTSD. The Opiate Treatment Index (OTI; Darke et al., 1992) and the Composite International Diagnostic Interview (CIDI; Robins et al., 1988) were used to collect information on substance use, and the Clinician Administered PTSD Scale (CAPS; Blake et al., 1995) was used to assess lifetime and current diagnosis of PTSD symptoms. Criminal activity was measured using the Crime Section of the OTI. The Buss-Perry Aggression Questionnaire (BPAQ; Buss & Perry, 1992) was used to assess aggression, anger and hostility.

**Results:** Preliminary analysis found that 39% of participants had a prison history and 74% had an arrest history. Twenty percent of participants had committed violent crime in the preceding month. Those who had committed violent crime used substances more frequently than those who had not committed violent crime. These individuals also had greater PTSD symptom severity and, in particular, greater severity of PTSD-related arousal symptoms. They also had elevated levels of aggression on the BPAQ, particularly on the anger and hostility subscales.

**Conclusions:** These findings provide preliminary support for the relationship between substance use, PTSD (arousal symptoms in particular) and violent crime. Knowledge of the factors that predispose individuals to criminal offending has important implications for clinical and forensic practitioners.

**Support:** The Australian National Health and Medical Research Council

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**NON-MEDICAL USE OF PRESCRIPTION OPIOIDS AMONG VETERANS WITH AND WITHOUT HIV: PAIN, PSYCHIATRIC, MEDICAL AND SUBSTANCE USE CORRELATES.**

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**Aims:** Background: Despite the growing awareness of the adverse effects of non medical use of prescription opioids (NMU), few research studies have systematically evaluated NMU among veterans with and without HIV. Aim: To examine the prevalence and correlates of NMU among a large sample of veterans in care. Hypotheses: Patients with NMU would exhibit significantly higher pain scores and more psychiatric, medical and substance use morbidity.

**Methods:** We analyzed self-report data from 4,122 participants in the Veterans Aging Cohort Study, an observational study of HIV-infected and uninfected veterans at eight sites. Data Analysis: Group differences were examined using chi-square tests, t-tests, and median tests for non-normally distributed data. Multivariable associations were assessed using logistic regression.

**Results:** Median participant age was 52 years; 95% were men, 65% described themselves as black. Thirteen percent reported past year NMU. Patients with NMU were more likely to be under age 55 (14 vs. 11%) and Hispanic (13 vs. 8%), and to have higher pain scores, PTSD (16 vs. 10%), major depressive disorder (21 vs. 14%), Hepatitis C (HCV; 40 vs. 22%), HIV (14 vs. 11%), an opiate medication prescription (9 vs. 5%), and a substance use disorder (46 vs. 22%);  $p < .05$  for all comparisons. In a multivariable model, NMU was associated with: being Hispanic (AOR 1.8, 95% CI 1.2-2.6); higher pain scores (1.1, 95% CI 1.0-1.1); PTSD (AOR 1.4, 95% CI 1.1-1.8); HCV (AOR 1.6, 95% CI 1.3-2.1); receipt of an opiate medication (AOR 1.8, 95% CI 1.3-2.6); drinking alcohol  $\geq 2$  times per week (AOR 1.4, 95% CI 1.1-1.8); and a substance use disorder (AOR 2.3, 95% CI 1.8-3.1).

**Conclusions:** Veterans in care are nearly three times as likely as adults in the general population to report NMU and they may benefit from interventions that address pain interference, and psychiatric, medical and substance use comorbidity.

**Support:** NIAAA U10AA013566-08, VA Research Enhancement Award Program and NIDA R01 DA019511-03, K23 DA024050-01

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### FEMALE VS. MALE PROLACTIN RESPONSE TO DYNORPHIN A1-13 IN NORMAL VOLUNTEER AND COCAINE-DEPENDENT SUBJECTS.

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**Aims:** Dynorphin A1-13 is a kappa opioid receptor agonist with poor penetrance across the blood-brain barrier. We have previously shown that dynorphin A1-13 causes a rapid increase in serum levels of prolactin, which may be used as a biomarker for tuberoinfundibular dopaminergic (TID) activity. Therefore, this natural sequence peptide can be used as probe of kappa opioid receptor activity and TID tone within the hypothalamus and pituitary. In an earlier study with a small number of female subjects (3), we found that healthy females had a greater prolactin response to dynorphin than males. We have expanded our studies in healthy volunteers and studied the response of cocaine dependent subjects.

**Methods:** On three separate days, intravenous doses of dynorphin A1-13 (0 µg/kg, 120 µg/kg, and 500 µg/kg) were used to determine prolactin response in normal volunteers (18 male and 18 female), and in cocaine dependent subjects (6 male and 3 female), studies initiated 1 to 10 days after last cocaine use in the cocaine dependent group.

**Results:** Normal volunteer women had higher basal prolactin levels than normal volunteer men ( $p < 0.02$ ); each gender showed a dose dependent increase in prolactin response to dynorphin. Two-way analysis of variance, group x gender, showed that, overall, cocaine dependent subjects had lower basal prolactin than normal volunteers, ( $p < 0.05$ ). However, response of the cocaine dependent group to dynorphin did not differ from that of the normal volunteers.

**Conclusions:** These results extend and confirm our earlier finding of higher basal prolactin levels and dynorphin response in female volunteers than in males. Cocaine dependent subjects showed no difference in prolactin response to dynorphin, unlike our finding in methadone maintained former heroin addicts.

**Support:** NIH-NIDA DA-P60-05130; NIH RR ULRR0204143

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### FIVE YEAR FOLLOW-UP OF A GROUP OF BRAZILIAN ECSTASY USERS: IS MDMA USE A TRANSIENT PHENOMENON?

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**Aims:** to determine the natural course of Ecstasy (MDMA) use within a five year timeframe in a sample of Brazilian young adults.

**Methods:** A qualitative approach was utilized to assess changes in Ecstasy use patterns from 2001 (n=32) to 2005/2006 (n=21). Sampling was intentional and occurred in Sao Paulo, Brazil. Data collection occurred through semi-structured interviews. Snow-ball technique was implemented. Nine subjects could not be reached and two declined to be re-interviewed. Shifts in Ecstasy use were examined in a prospective longitudinal design. Patterns of DSM-IV defined ecstasy abuse and dependence.

**Results:** Subjects average age was 24,9 years in baseline and 28,7 years in follow-up. From 2001 to 2005/2006, three scenarios emerged: (A) Transient use group (n=14) either quit using ecstasy or cut it down significantly (more than 50%); (B) Long term habitual use (n=6) maintained or cut slightly down MDMA use (less than 50%); (C) Compulsive use group (n=1) increased in more than 50% ecstasy use within timeframe. Alcohol and marihuana consumption remained unaltered within the timeframe. Furthermore, four respondents referred increases in cocaine use and six subjects mentioned initiation in crystal methamphetamine use. As changes in life cycle occurred, a group of respondents matured-out of MDMA use, as part of a transient and youth-limited phenomenon. Another group of subjects' maintained lifestyle unaltered as clubbing and social life remained focused. MDMA use persisted and was part of a 'work hard-play hard' ethos.

**Conclusions:** After a five year timeframe, MDMA use manifested as a transient phenomenon for part of the respondents. Nevertheless, for a smaller group, it manifested as a lasting experience. Public health policies should target ecstasy use accordingly with youth-focused preventive strategies and a harm reduction approach.

**Support:** This study was supported by FAPESP (Fundo de Amparo à Pesquisa no Estado de São Paulo)

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### MEDICAL COMORBIDITY AND HCV TREATMENT ELIGIBILITY IN METHADONE MAINTENANCE TREATMENT VS NON-METHADONE MAINTENANCE TREATMENT PATIENTS SEEKING TREATMENT FOR HCV INFECTION.

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**Aims:** Comorbid medical illness is common in patients with either chronic hepatitis C (HCV) infection or opioid dependence undergoing methadone treatment (MMT). However, little is known about the additive impact of opioid dependence and MMT patient status on medical comorbidity and eligibility for HCV treatment.

**Methods:** 80 MMT and 80 non-MMT patients seeking treatment for chronic HCV infection and matched for age, gender, and race, were compared on comorbid chronic medical diagnoses, Cumulative Illness Rating Scale (CIRS-M) scores, and HCV treatment eligibility. The MMT patients were participants in a NIDA-funded HCV treatment study.

**Results:** Both groups were similar in HCV genotype distribution and HCV viral load. Similarly high proportions of each group had comorbid chronic medical conditions: 91% of MMT and 85% of non-MMT patients. Both groups averaged 3 comorbid medical conditions per patient, yet overall CIRS-M medical severity scores were low in both groups. There was a trend [ $p = .06$ ] toward a higher rate of HCV treatment eligibility in the non-MMT group (78%) than in the MMT group (63%); this difference was significant for patients with HCV genotypes 1 and 4 [ $p \leq .01$ ]. Comorbid medical illness led to treatment ineligibility in 18% of MMT and 16% of non-MMT patients [ $p = NS$ ]. Failure to complete the medical evaluation process was significantly [ $p \leq .001$ ] more likely to be the cause of ineligibility for MMT patients.

**Conclusions:** MMT and non-MMT patients seeking HCV treatment had comorbid medical illnesses of similar number and severity. However, fewer MMT patients were eligible for HCV treatment — not because of greater comorbid medical problems, but because MMT patients were more likely to be ineligible due to failure to complete the required medical evaluation process despite participation in an HCV treatment study.

**Support:** NIDA R01 DA016764

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### NON-LINEAR KINETICS OF (±)-3,4-METHYLENEDI OXYMETHAMPHETAMINE IN RATS.

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**Aims:** Based on preclinical evidence, there is speculation that (±)-3,4-methylenedioxymethamphetamine (MDMA, or Ecstasy) is toxic to humans. Extrapolation of toxicity data from animals to humans requires detailed assessment of pharmacokinetics across species. Here we examined the effects of dose and route on pharmacokinetics of MDMA in male rats.

**Methods:** Catheterized rats received low-dose (2 mg/kg) or high-dose (10 mg/kg) MDMA via i.p., s.c. or p.o. routes. Repeated blood samples were collected, and plasma was assayed for MDMA and its metabolites, 4-hydroxy-3-methoxymethamphetamine (HMMA) and 3,4-methylenedioxymphetamine (MDA), by gas chromatography/mass spectroscopy.

**Results:** After 2 mg/kg, MDMA C<sub>max</sub> values were ~200 ng/mL for i.p. and s.c. routes but less for the p.o. route. Plasma half-life of MDMA was < 1 h in all groups, and route did not affect time-concentration profiles of HMMA or MDA. After 10 mg/kg, MDMA area-under-the-curve (AUC) values were 21-fold (i.p.), 10-fold (s.c.) and 36-fold (p.o.) higher than values at 2 mg/kg. By contrast, HMMA AUC values after 10 mg/kg were < 3-fold greater than at 2 mg/kg.

**Conclusions:** Administration of low-dose MDMA to rats produces C<sub>max</sub> concentrations similar to those reported in humans. HMMA is a major metabolite in rats while MDA is less prevalent. Analogous to clinical findings, MDMA displays non-linear kinetics in rats, and this phenomenon appears to involve impaired drug metabolism. Taken together, our data show similarities between MDMA kinetics in rats and humans.

**Support:** Generously funded by NIDA/IRP, NIH, DHHS.

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### IS EARLY ALCOHOL AND NICOTINE USE ASSOCIATED WITH THE RISK OF CANNABIS USE AND TRANSITION TO CANNABIS USE DISORDERS IN ADOLESCENCE?

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**Aims:** Background: Adolescents are likely not naive to alcohol use (AU) and nicotine use (NU) at first cannabis use (CU). However, the role of prior AU and NU for CU onset and progression to cannabis use disorders (CUD) in adolescence remains understudied.

**Aims:** To (1) identify the sequence of and latency between initial AU/NU and CU. To assess, whether (2) early AU/NU is related to CU and to early CU onset (3) early AU/NU is related to a higher risk and speed of transition from first CU to CUD.

**Methods:** Methods: N=3,021 community subjects aged 14-24 at baseline were followed up prospectively over up to ten years. Substance use and CUD were assessed with the DSM-IV/M-CIDI.

**Results:** Results: (1) Most subjects with CU reported AU (99.6%) and NU (94.7%). Among users of both substances, 93% reported AU and 87.5% reported NU as prior to CU. At one year after first AU, 10% of all transitions to CU had occurred and at one year after first NU 10 - 20% of transitions to CU had occurred. (2) Early AU and NU were associated with any and with especially early CU: Alcohol users with CU had on average a 0.67 years earlier AU onset (95% CI: 0.4 - 0.9) in comparison to those without CU. Subjects with NU and CU had a 0.60 years earlier NU onset (95% CI: 0.3 - 0.9). Earlier AU onset was related to a 0.17 years earlier CU onset on average (95% CI: 0.1-0.2). Earlier NU onset was related to a 0.30 years earlier CU onset (95% CI: 0.2-0.4). (3) AU before age 15 was associated with a higher risk of cannabis abuse. NU before age 16 was related to a higher risk of cannabis dependence. AU before age 11 was related to a faster transition to cannabis dependence.

**Conclusions:** Conclusion: AU and NU do not simply occur prior to CU. Specific features of AU and NU as early onset are associated with critical steps of CU development. Preventing early AU/NU may serve as an early preventive strategy for CU and CUD.

**Support:** Supported by: BMBF

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### DESCRIBING THE GAMBLING TREATMENT WORKFORCE: A SURVEY TO EXPLORE AN UNEXAMINED POPULATION.

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**Aims:** In order to disseminate empirically supported assessment tools and treatment protocols for gambling-related disorders, it is important to understand the nation's treatment providers' demographic characteristics, professional qualifications, training needs, and readiness to adopt evidence-based practices. Although the need for this information has been identified (Clark, 2005), no national study of the gambling treatment workforce has been conducted to date.

**Methods:** A web based workforce survey was developed to collect data from a national sample of professionals who treat people with problem gambling disorders. Approximately 216 problem gambling treatment providers from 25 states completed the survey.

**Results:** 216 problem gambling treatment providers from 26 states filled out the survey. The average age of treatment providers is 49 years old. 122 providers, or 56% have their Masters degree and 69% have 0-6 years experience treating problem gambling. Respondents were given a definition of evidence based practices (EBP) and asked how clear they felt their understanding was of EBP. 81% reported feeling somewhat to completely clear in their understanding of EBP prior to reading the definition; 77% reported understanding research findings in peer reviewed journals all or most of the time; 77% would like to see more EBP adopted in their agencies.

**Conclusions:** This survey will provide baseline information that will contribute significantly to our understanding of the gambling treatment workforce and inform efforts to implement empirically validated treatment methods.

**Support:** This project was supported by funding from the National Center for Responsible Gaming as provided by The Institute for Research on Pathological Gambling and Related Disorders in the Division on Addictions at Cambridge Health Alliance. Its contents are solely the responsibility of the author(s) and do not necessarily represent the official views of the National Center, the Institute, or Cambridge Health Alliance.

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### INTRAHYPOTHALAMIC ADMINISTRATION OF GP120 INDUCES FEVER VIA CXCR4 RECEPTORS.

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**Aims:** Wasting syndrome is a common complication of HIV infection and is marked by progressive weight loss and weakness, often associated with diarrhea and fever. The mechanisms involved in the pathogenesis of these syndromes are not well defined, and neither are the brain areas involved. The present study tests a new hypothesis: that the preoptic anterior hypothalamus (POAH), the main brain area for thermoregulation and fever, has a role in the pathogenesis of fever induced by gp120 and that the CXCR4 receptors that serve as a co-receptor for HIV entry, mediate the effect.

**Methods:** Male S-D rats weighing 250-300 g were used, 8-10 rats per group. A sterilized stainless steel C313G cannula guide (22 gauge, Plastics One Inc., Roanoke) was implanted into the POAH, and a biotelemetry system was used to monitor the body temperature changes.

**Results:** The administration of gp120 (33 to 133 ng) into the POAH induced fever in a dose-dependent manner. To demonstrate the possible links between the gp120 and CXCR4 in generating the fever, we pretreated the rats with AMD3100, an antagonist of SDF-1beta /CXCL12, acting at its receptor, CXCR4, 30 min prior to administration of gp 120. AMD 3100 significantly reduced the gp120-induced fever, particularly during the first 2 hours.

**Conclusions:** The present studies show that: 1) The POAH is involved in the pathogenesis of the fever induced by gp120 and 2) in the POAH, gp120 interacts with the chemokine system to generate the fever associated with gp120.

**Support:** (Supported by Grants DA06650 and DA13429)

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### ALTERATIONS IN THE DENSITY OF GROUP II MGLURS IN THE STRIATUM OF NONHUMAN PRIMATES FOLLOWING CHRONIC COCAINE SELF-ADMINISTRATION.

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**Aims:** Though research into the consequences of chronic cocaine exposure has focused on monoamine systems, recent evidence has suggested an additional impact on glutamate systems. Glutamate has a prominent role in synaptic plasticity and the remodeling of synapses, thus alterations within this system may have significant consequences. Rodent studies have shown decreases in the function of metabotropic group II glutamate receptors (mGluRs) in the nucleus accumbens following chronic cocaine exposure. Group II mGluRs are inhibitory receptors that can act as autoreceptors when located presynaptically, thereby inhibiting glutamate release. To determine whether group II mGluRs are affected in nonhuman primates, as in rodents, we measured the density of group II mGluRs in the striatum of monkeys following chronic cocaine exposure.

**Methods:** Monkeys (N=4) self-administered cocaine (fixed interval 3-minute schedule, 0.3 mg/kg/infusion) for a period of 100 days (30 reinforcers per day). Control animals (N=6) responded for food-reinforcement under the same schedule and for the same period of time. Following the final reinforcer, brains were removed, frozen in cooled isopentane and cut on a cryostat (20 µm sections) and stored at -80°C before use. Binding to group II mGluRs in the striatum was determined using [3H]LY341495.

**Results:** Significantly higher densities of group II mGluRs were measured in the dorsolateral (25%), dorsomedial (13%) and ventromedial (14%) caudate nucleus in animals chronically self-administering cocaine compared to controls, though, in contrast to rodent data, no significant differences were observed in either the nucleus accumbens or putamen.

**Conclusions:** These findings indicate that group II mGluRs are altered as a direct consequence of chronic cocaine exposure, potentially leading to impaired regulation of glutamate transmission. This may ultimately result in dysfunction in plasticity and synaptic remodeling, which is believed to underlie the adaptations that occur following chronic drug use.

**Support:** DA09085 DA06634

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# INHIBITION OF G $\beta$ $\gamma$ SIGNALING TO PHOSPHOLIPASE $\beta$ 3 ENHANCES ANTINOCICEPTION MEDIATED BY THE $\mu$ OPIOID RECEPTOR BUT DOES NOT AFFECT RESPIRATION OR LOCOMOTION.

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**Aims:** Previously, the compound M119 was shown to inhibit signaling from the G $\beta$  $\gamma$  subunit to phospholipase  $\beta$ 3 (PLC $\beta$ 3) and this inhibition shifted the morphine analgesic dose-response curve to the left, but did not have any effect on antinociception mediated by  $\delta$  or  $\kappa$  opioid receptors (Mathews et al., J. Neurosci. 28:12183, 2008). Gallein has a chemical structure that is very similar to M119 and has been shown to inhibit G $\beta$  $\gamma$  signaling. The aim of this study was to determine if inhibition of G $\beta$  $\gamma$  signaling to PLC $\beta$ 3 would affect morphine-induced respiratory depression and locomotion.

**Methods:** The 55°C warm-water tail flick test was used to measure morphine-induced antinociception in mice. Gallein was administered 10 min before morphine and both compounds were administered by an i.p. injection. The CLAMS monitoring system (Columbus Instruments) was used to measure breathes per min and ambulations per min over a 90-min time course with C57Bl/6 mice. Data were compared to saline-treated controls and to mice that received only morphine or only gallein.

**Results:** Gallein enhanced morphine-induced antinociception in the mouse 55°C warm water tail flick test. The duration of morphine-induced antinociception was prolonged in mice treated with gallein and morphine in comparison to mice treated with only morphine. However, gallein did not increase morphine-induced respiratory depression or locomotion in comparison to morphine alone.

**Conclusions:** By inhibiting G $\beta$  $\gamma$  signaling to PLC $\beta$ 3, gallein increased both the magnitude and duration of morphine-induced antinociception. However, gallein did not increase morphine-induced respiratory depression or locomotion, suggesting that G $\beta$  $\gamma$  signaling to PLC $\beta$ 3 does not mediate morphine-induced respiratory depression or locomotion. These results suggest that it may be possible to increase analgesia mediated by the  $\mu$  opioid receptor by inhibiting G $\beta$  $\gamma$  signaling to PLC $\beta$ 3 without affecting either respiration or locomotion.

**Support:** Supported by K05-DA00360 and the Margo Cleveland Fund.

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# ABUSE DETERRENT ADJUSTED MEASUREMENT MODEL: ADAMM<sup>TM</sup>

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**Aims:** The abuse of prescription opioid medications has placed an impetus on pharmaceutical companies to develop so-called abuse deterrent formulations (ADFs) for opioid medications. It is critical to establish methods to determine the impact of such formulations on actual abuse rates. ADAMM<sup>TM</sup> is proposed as an approach for assessing the odds of abuse for an ADF in relation to appropriate comparators. The goal of this study is to provide an initial test of ADAMM<sup>TM</sup> by examining the odds of abusing an existing drug, OxyContin®, in relation to: (1) Duragesic®, (2) MS Contin®, and (3) Vicodin® using NAVIPPRO<sup>TM</sup> data from patients seeking substance abuse treatment across the U.S.

**Methods:** Data from 3,516 patients in substance abuse treatment representing 47 3-digit home zip codes, were analyzed. A multilevel logistic regression analysis estimated the odds ratio of abusing OxyContin® vis-à-vis the comparator medications.

**Results:** Results revealed the odds of abusing OxyContin® was 9.77 times the odds of abusing Duragesic® (95% CI: 6.71, 14.23), 1.15 times the odds of abusing MS Contin® (95% CI: 0.45, 1.57), and 0.33 times the odds of abusing Vicodin® (95% CI: 0.26, 0.41), after adjusting for local, prescribed availability. Local availability was defined as the total number of morphine equivalent grams dispensed by pharmacies during the current and previous two months divided by the population density in each 3-digit patient home zip code area.

**Conclusions:** These results illustrate a model that appears to be capable of determining the odds of abusing one prescription opioid compared to another after adjusting for local availability of the product. As ADFs enter the market, this model will permit direct comparison of an ADF with appropriate comparators adjusted for local, dispensed availability. Since "abuse deterrence" may be a dynamic characteristic (e.g., it may change over time), ongoing monitoring of an ADF's odds of abuse with respect to comparators will be essential. This model shows promise as way of evaluating an ADFs public health impact.

**Support:** Inflexxion, Inc.

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# A BOLD FMRI STUDY OF CANNABINOID ACTION IN RAT BRAIN.

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**Aims:** Cannabinoid action encompasses many physiological and behavioral systems in the brain. The aim of this study is to elucidate sites of action of delta<sup>9</sup>-tetrahydrocannabinol (THC) and other cannabinoids, in the rat brain and determine those mechanistically related to their pharmacological actions. The effects of THC and cannabidiol (CBD) are presented here.

**Methods:** Under isoflurane anesthesia, rats were prepared for imaging. After surgery, anesthesia was switched to iv medetomidine, which produces deep sedation and analgesia, and maintained during scanning. Pancuronium was used to induce paralysis and minimize motion artifacts. fMRI experiments were performed using a Bruker Medspec 9.4 T scanner A single-shot EPI sequence (slice thickness 1 mm) was used for all functional imaging. THC (0.3–4 mg/kg) and CBD (10 mg/kg) were given iv and scanning performed for 70 min after drug administration. Forepaw electrical stimulation was also performed prior to and 30 and 60 min after drug treatment.

**Results:** THC produced time-related changes in fMRI signal (brain activity) in regions of the brain predicted from the distribution of CB1 receptors. Dose-related differences in hippocampus were seen. The 0.3 mg/kg dose produced a small increase in activity, while 4 mg/kg produced a decrease. The 0.3 mg/kg dose also produced a significant increase in the n. accumbens which was not seen with higher doses or vehicle. CBD produced neither effect. Forepaw stimulation produces robust repeatable activation of somatosensory cortex that is not altered by drug treatment. However, CBD produces a significant overall decrease in MR signal in that cortical region, not seen with THC.

**Conclusions:** These results indicate that BOLD fMRI is a sensitive measure of regional differences in cannabinoid action in rat CNS. The large area of negative activation proximal to the somatosensory cortex activated by forepaw stimulation, seen after CBD suggests that CBD is able to potentiate inhibitory mechanisms engaged in response to intense repetitive stimulation, pointing to possible uses of CBD-like drugs.

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# REGIONAL VARIATIONS AND FACTORS ASSOCIATED WITH LATE INJECTION DRUG USE INITIATION IN CALIFORNIA.

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**Aims:** Background: Drug prevention efforts have been focused on drug use initiation among youth and young adults. Less attention has been paid to escalation from less dangerous to more dangerous drugs or to drug use via more dangerous administration routes (e.g. injection). Little information is known about the prevalence and risk factors for late injection drug use initiation. Objective: To assess whether region and other factors were associated with injection drug injection among injection drug users in a cross-sectional sample of California syringe exchange program clients.

**Methods:** Methods: The California Syringe Exchange Program (CalSEP) study collected drug use and HIV risk data from ~1,600 injection drug users (IDUs) at 24 programs from 2001-03. Respondents who reported initiation of injection drug use during their thirties or later were classified as late initiators. We examined regional variations in late initiation in 5 California regions (Northern, SF Bay Area, Central Coast/Central Valley, Los Angeles, and San Diego) and other factors associated with late initiation.

**Results:** Results: There was no significant regional variation in late initiation (range 18.4% to 23.1%). In multivariate analysis, IDUs who reported any heroin (Adjusted Odds Ratio[AOR]=0.53, p<0.01) or speedball use (AOR=0.52, p<0.01) were less likely to be late initiators as were men (AOR=0.54, p<0.01). As compared to African Americans, Hispanics (AOR=0.39, p<0.01), Native Americans (AOR=0.38, p=0.03), and other race/ethnicity (AOR=0.32, p=0.04) were less likely to be late initiators. Late initiators as compared to other IDUs did not differ in terms of HIV risk or readiness for drug treatment.

**Conclusions:** Conclusion: Late initiation appears widespread, yet little is known about late initiators and risk factors for late drug injection initiation. Research is needed to develop late injection initiation profiles, prevention strategies, and drug treatment options.

**Support:** CDC grant# 918667 & NIDA grant#RO1 DA1420

**CONDITIONAL ODDS OF RECENT DRUG USE DISORDERS IN RELATION TO PTSD HISTORY: USA, 2004-5.**

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**Aims:** To estimate the hypothesized association that links a past history of post traumatic stress disorder (PTSD) with recent drug use in a community sample of trauma victims.

**Methods:** Data are from wave 2 of the USA National Epidemiologic Survey on Alcohol and Related Conditions, with 34,653 community-dwelling adult participants assessed during 2004-5, 92% of whom had experienced DSM-IV traumatic events. Standardized diagnoses for DSM-IV lifetime PTSD and recent (past-year) DSM-IV drug use disorders were made via the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS). Weighted logistic regressions produced study estimates from models in which the odds of nicotine, alcohol, and other drug use disorders among the trauma-exposed were regressed on the PTSD history, with covariate adjustments for sex, age, race/ethnicity, and educational level.

**Results:** An estimated 14%, 10%, and 2% qualified as recent nicotine, alcohol, and other drug use disorder cases, respectively. With covariates held constant in a comparison of adults with and without PTSD history, recent drug use disorders were associated with PTSD history (nicotine: adjusted odds ratio, AOR=2.3; 95% confidence interval, CI =2.1, 2.6; alcohol: AOR=1.7; 95% CI=1.5, 2.0; other drugs: AOR=2.8; 95% CI=2.2, 3.6).

**Conclusions:** According to these epidemiological data, a PTSD history might influence onset of the drug use disorders under study, and also might promote the duration of drug use disorders. Prospective research and time-to-event analyses can be used to sort out these distinctions.

**Support:** This work was supported by grants F31 DA021040 and K05 DA015799 from the National Institute on Drug Abuse.

**METHAMPHETAMINE IMPAIRS SEXUALLY CONDITIONED APPROACH IN MALE JAPANESE QUAIL.**

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**Aims:** The present study aimed to investigate the effects of chronic pre-exposure to methamphetamine on locomotor activity, approach to a conditioned stimulus (CS) paired with sexual reinforcement, and sexual performance.

**Methods:** Male Japanese quail (N = 34) received saline or methamphetamine (3.0 or 5.6 mg/kg i.p.) once-daily for 10 days and locomotor activity was measured. After a 31 day withdrawal period, male quail were presented a red light (CS) just prior to a copulatory opportunity with a female quail (US) once-daily for 14 days. Time spent near the CS and general locomotor activity was measured during sexual conditioning tests. Unpaired quail were given a copulatory opportunity 3-4 hrs prior to each sexual conditioning test and were not allowed to copulate with a female following presentation of the CS.

**Results:** Subjects that received 5.6 mg/kg i.p. methamphetamine displayed a significant decrease in locomotor activity from trial 1 to trial 10 ( $F(2, 31) = 3.415$ ,  $p = 0.046$ ). Paired quail spent more time near the CS than unpaired quail ( $F(1, 28) = 9.128$ ,  $p = 0.005$ ). Paired quail pre-exposed to 3.0 mg/kg i.p. methamphetamine showed decreased approach to the CS relative to paired saline controls ( $F(26, 364) = 1.425$ ,  $p = 0.084$ ). Paired quail that received 5.6 mg/kg methamphetamine and saline displayed enhanced general locomotor activity during sexual conditioning tests. Compared to saline controls, quail pre-exposed to methamphetamine did not display impaired sexual performance or copulatory efficiency. Paired quail were more efficient at copulation than unpaired quail ( $F(1, 28) = 12.003$ ,  $p = 0.002$ ).

**Conclusions:** The results of the current study suggest that chronic pre-exposure to 5.6 mg/kg i.p. methamphetamine may induce locomotor tolerance. Moreover, pre-exposure to methamphetamine 3.0 mg/kg appeared to impair the development of conditioned approach relative to saline, but this effect was not observed with a higher dose (5.6 mg/kg i.p.). Overall, chronic pre-exposure to methamphetamine dose-dependently impaired sexually conditioned approach but had no effect on sexual performance or copulatory efficiency.

**Support:** Support provided by NIDA grant DA00508.

**DRUG COMBINATIONS SEIZED BY LAW ENFORCEMENT, EMERGING TRENDS AND UNDETERMINED EFFECTS TO THE UNSUSPECTING USER.**

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**Aims:** The use and abuse of mind altering substances remains a continual health and law enforcement issue. New drug combinations rapidly emerge on the illicit market with little warning, evident by rapid occurrence of fentanyl combined with heroin and cocaine resulting in an excess of 1000 deaths between 2005 and 2007. In addition to establishing identity and origin, seized drugs are qualitatively analyzed to monitor trends.

**Methods:** Data from these analyses is maintained by the System to Retrieve Investigational Drug Evidence (STRIDE) and National Forensic Laboratory Information System (NFLIS), documenting the prevalence and proportionalities of these dangerous drug combinations.

**Conclusions:** The acute and long-term effects of these drug combinations are unknown and demand a closer analysis. The synergism of these drugs may produce unique adverse effects; thus, increased awareness of the effects of specific adulterants is warranted.

**Support:** Ecstasy tablets continue to be found as complex chemical mixtures, adulterated with a range of drug combinations including methamphetamine, caffeine, TFMP, ketamine, PMMA, diazepam, phenobarbital, and many others. Other drug combinations such as heroin-clenbuterol, methamphetamine-isopropylbenzylamine, and cocaine-levamisole have been increasing in prevalence in the illicit drug market.

**THE MEXICAN MIGRATION TO THE U.S. AND SUBSTANCE USE IN NORTHERN MEXICO.**

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**Aims:** To examine the impact of migration to the US on substance use and substance use disorders in three urban areas of Northern Mexico.

**Methods:** Cross-sectional survey of immigration related experiences and lifetime and past-year alcohol and drug use, in a representative sample of respondents ages 12 to 65.

Interviews were conducted in the cities of Tijuana, Ciudad Juarez, and Monterrey during 2005. Respondents were classified into three groups: 1) "return migrants", 2) "relatives of migrants" and 3) "others in the general population".

**Results:** A total of 1,630 completed interviews were obtained for a response rate of 70.5%. "Return migrants" were more likely to have used alcohol, marijuana or cocaine at least once in their lifetime and in the last 12-months, more likely to develop a substance use disorder, and more likely to have a 12-month substance use disorder, compared with "others in the general population". Among "return migrants", longer length of time in the US and type of work performed as an immigrant were related to higher prevalence of substance use. Among "relatives of migrants", migration experiences were not associated with increased prevalence of substance use compared with "others in the general population".

**Conclusions:** This study found a link between migration to the US and the transformation of substance use norms and pathology in Mexico. Future research of pre-migration involvement in substance use and data on the timing of events among return migrants is needed. Public health measures are likely to require cross-border coordination of research and service development.

**Support:** This research was possible due to support from the Consejo Nacional contra las Adicciones (CONADIC) and Consejo Estatal contra las Adicciones de Baja California, Chihuahua y Monterrey.

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**SOCIAL DISCOUNTING AMONG PREGNANT CIGARETTE SMOKERS.**

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**Aims:** Temporal discounting is of growing interest because of its ability to discriminate the presence and severity of substance use disorders (SUDs). The present study aims to investigate another type of discounting, namely social discounting. In social discounting the subjective value of individuals in one's social network is discounted as a function of steps of social separation ranging from being very close emotionally to mere acquaintances. The present study was conducted as a first effort to examine whether degree of social discounting might discriminate between women who quit vs. continue smoking during pregnancy.

**Methods:** Subjects were 77 pregnant women who reported being smokers at the time of conception; 61 were still smoking upon entering prenatal care while 16 quit shortly after learning of the pregnancy. To assess social discounting, participants listed 100 people in their social network and ranked them from emotionally close to distant (Jones & Rachlin, 2006). Then they were asked to answer a series of written questions concerning various amounts of hypothetical money to be kept for themselves (selfish option) or shared with different persons on their list (sharing option). A crossover value where individuals switched from the shared to selfish options was determined at increasing levels of social distance.

**Results:** Similar to temporal discounting, a hyperbolic model provided a better fit to the average crossover data than did an exponential model ( $R^2=.96$  vs.  $R^2=.81$ ). Women who continued smoking were significantly steeper social discounters than those who quit ( $s=.099$  vs.  $s=.046$ ,  $p < .05$ ). Additional analyses are planned prior to the conference.

**Conclusions:** Greater social discounting among smokers as shown in the present study may lessen the influence of social efforts to discourage smoking during pregnancy or perhaps be indicative of a lesser concern among continuing smokers about effects of their behavior on others, including their fetus. Further research examining social discounting among pregnant women with SUDs appears warranted.

**Support:** R01 DA14028 and T32 DA07242-17 from NIDA

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**IS PREGABALIN (LYRICA®) A DRUG OF ABUSE OR PROTECTION AGAINST DRUG ABUSE? A COMPARISON WITH GABAPENTIN WITHIN THE NORWEGIAN PRESCRIPTION DATABASE.**

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**Aims:** Pregabalin is a novel antiepileptic also used for the treatment of pain and anxiety. There are reports on benzodiazepine abuse reduced after upstart with pregabalin. There have, however, also been reports on pregabalin being abused, and sold on the street. We wanted in a nationwide complete prescription database to investigate pharmacoepidemiological parameters for use and abuse of pregabalin and compare these to gabapentin, an older, but similar antiepileptic.

**Methods:** Data were drawn from the NorPD. All Norwegian citizens who had received at least one prescription for either pregabalin or gabapentin 2004-7 and were between 18 and 69 were included. No diagnosis was available. Patients were grouped as psychiatric patients, epileptics, neuropathic pain patients or others according to the reimbursement code and the prescribing doctor's specialty. Indication of abuse was measured by skewness in use. A Lorenz curve was constructed. Amount of benzodiazepines used 6 months before and after upstart with pregabalin was measured.

**Results:** The Lorenz 1 % measures how much of the drug is prescribed to the 1 % using the most and was rather similar between pregabalin and gabapentin. However, as much as 19.6 % of pregabalin were prescribed to the 1 % highest users in the "other" group, indicating abuse. About 20 % of the patients starting pregabalin treatment stopped using benzodiazepines. Psychiatric patients starting pregabalin treatment reduced their use of benzodiazepines with 50 % in the 6 months after upstart.

**Conclusions:** Pregabalin behaved very similar to the older gabapentin in these investigations. Prescribed under controlled circumstances by specialists in the field, the use of these drugs could prove advantageous in reducing use of benzodiazepines.

**Support:** This work was sponsored by internal funding only

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**LOS ANGELES YOUTH COLLABORATIVE FOR SUBSTANCE USE AND VIOLENCE PREVENTION AMONG GANG EXPOSED YOUTH.**

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**Aims:** Los Angeles Youth Collaborative (LAYC): Gang Reduction and Youth Development is the first of its kind bringing faith and community agencies together for culturally competent substance use prevention, violence prevention and gang reduction initiatives.

**Methods:** Over 3 years, prevention services will be provided to 300 African American and Latino youth between the ages of 10 and 15 who are most vulnerable to joining a gang. Programming will be delivered after school and provide "safe passage" for youth and families to attend.

**Results:** LAYC is an evidence-based after school substance use prevention, gang prevention and violence prevention program set in the faith-based communities in South Los Angeles. Los Angeles Metropolitan Churches, with funding from the City of Los Angeles Mayor's Office of Gang Reduction and Youth Development (GRYD) Prevention Services, has partnered with community organizations having over fifty years experience in youth substance and violence prevention services to deliver the program. Two curriculums will be implemented: one curriculum is the Refuse Explain Avoid Leave (REAL) for substance use prevention; the second curriculum is: Second Step®: A Violence Prevention Curriculum designed to reduce impulsive and aggressive behavior in children by increasing their social competency skills.

**Conclusions:** Culturally competent prevention programming that targets urban youth can provide a structural framework for community- and faith-based organizations to address risk factors, while also reducing trajectories toward substance use, gang involvement and violence.

**Support:** This project is funded by the City of Los Angeles Mayor's Office of Gang Reduction and Youth Development (GRYD) Prevention Services (September 1, 2008 to June 30, 2010).

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**PRESCRIPTION OPIOID USE AMONG CONVICTED DRINKING DRIVERS.**

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**Aims:** Relatively little evidence exists on the prevalence of use of prescription opioids among high risk groups such as convicted drinking drivers who are known to be at elevated risk of collision involvement. In this study we examine self-reported use of prescription opioids among convicted drinking drivers.

**Methods:** Data are based on 22,277 convicted drinking drivers (88% males, mean age=44years) who completed Ontario's remedial program 'Back on Track' (BOT), including assessment and 6 month follow-up, between 2000 and April 30, 2005. Measures examined included numbers of days using alcohol and other drugs, average number of drinks per drinking occasion, number of substance-related problems experienced and number of users of each substance in the 90 days prior to the assessment and follow-up interviews. The substances examined were alcohol, cocaine, amphetamines, cannabis, benzodiazepines, barbiturates, prescription opioids and tobacco. Substance-related problems were measured by the Research Institute on Addictions Self Inventory, Alcohol Dependence Scale and the Drug Abuse Screening Test.

**Results:** The prevalence of prescription opioid use in the 90 days preceding assessment was 7.6%. Among drivers who reported use of only one prescription drug, the largest number reported using prescription opioids (1156), compared to 261 who reported using benzodiazepines. Drivers who reported using alcohol and prescription opioids but no other drugs had similar scores on problem measures to those who reported using alcohol alone, or alcohol and drugs other than prescription opioids. However, drivers who reported using alcohol, prescription opioids, and other drugs had significantly higher scores on all problem measures, suggesting that this group is at particularly high risk for subsequent problems.

**Conclusions:** Further research on the use of prescription opioids in this population is warranted.

**Support:** Funding was provided by Ontario's Back on Track Program.

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### OUTCOMES OF SUBSTANCE ABUSE TREATMENT ADJUSTING FOR SELECTION BIAS.

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**Aims:** These analyses examined substance abuse treatment outcomes from a statewide perspective, adjusting for the propensity to have incomplete outcome data (i.e., a type of "selection bias"). Data were from the first evaluation of the California Outcomes Measurement System. About half of the treatment episodes ending in fiscal year 2006-07 did not have outcome data recorded (e.g. due to treatment "drop out"); hence there was concern that evaluation of outcomes might present a biased picture. Hypotheses included: 1) propensity for missing outcomes is predicted from socio-demographic, substance use, and treatment characteristics at admission; and 2) adjusting for this selection bias will modify the assessment of change in substance use over time, but adjusted outcomes will remain significant.

**Methods:** Based on the sample of over 150,000 treatment episodes, logistic regression was used to predict missing outcome data and generate a propensity score. Generalized linear models for repeated measures assessed change in primary substance use from admission to discharge for the subsample with available outcomes, adjusting for the propensity from the first analysis.

**Results:** The sample was 64% male/36% female, 44% non-Hispanic White, 31% Hispanic, 14% African-American, and 11% other ethnicity. Primary substance was 37% methamphetamine, 19% alcohol, 15% marijuana, 16% opiates, 10% cocaine, and 3% other. Results showed that unavailability of outcome data was more likely for males, African-Americans and Hispanics, illicit substance users (compared to licit, i.e., alcohol), injection users, clients with more severe use at admission, or clients not referred through criminal justice sources. While this propensity was related to change in primary substance use, the propensity adjustment had little impact on the overall magnitude of change.

**Conclusions:** Results may identify clients vulnerable to non-completion of treatment and showed that adjusting for incomplete outcome data (selection bias) did not alter the overall assessment of substantial positive improvement from treatment admission to discharge.

**Support:** Evaluation contract from CA Dept. of Alcohol & Drug Programs

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### GENDER DIFFERENCES IN HIV RISK BEHAVIORS AMONG DRUG ABUSERS.

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**Aims:** This study examined gender differences in the rates and correlates of HIV sexual and drug risk behaviors in a sample of clients participating in 5 multi-site trials of the NIDA Clinical Trials Network.

**Methods:** HIV sexual risk behaviors and drug risk behaviors in the past 30 days were assessed at treatment entry. Measures of recent substance use, psychiatric severity, abuse history, social relations, legal involvement, and housing stability were examined in models predicting sex and drug risk behaviors.

**Results:** The sample of 1,429 individuals was 45% women. Participants were an average of 37 years old, 49% White, 37% African-American, and half (49%) were employed full-time. In the past 30 days, 39% used both opioids and stimulants, 21% used stimulants only, and 17% used opioids only. Men were more likely to report injection drug use. No other differences in drug risk behaviors were found. Women were more likely to report multiple partners, unprotected sex with regular partner, and greater engagement in high risk sexual behaviors overall. Greater alcohol use and psychiatric severity were associated with engagement in sex risk behaviors for women. Women with greater alcohol use engaged in higher drug risk behaviors. While impairment in social relations was related to less engagement in sex risk behaviors for men. Stimulant use, sexual abuse history, drug use severity, and legal involvement were associated with engagement in higher risk sexual behaviors for women and men.

**Conclusions:** Rising rates of HIV in women highlight the need to identify factors associated with risk behaviors in women. Women were less likely to report condom use with a regular partner, suggesting that condom use in an ongoing relationship may be discouraged by the male partner and reflect poorer negotiation skills. The association of alcohol use and psychiatric symptoms with risk behaviors may be the result of inferior negotiation skills or reflect social affiliation needs of vulnerable women.

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### TREATMENT VS NON-TREATMENT GROUPS: VALIDATION OF THE ADDICTION BELIEF INVENTORY.

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**Aims:** To evaluate the external validity of the Addiction Belief Inventory (ABI) (Luke, Ribisl, Ribisl, Walton, & Davidson, 2002) as a tool for assessing attitudes toward addiction among non-treatment populations.

**Methods:** The ABI was part of a larger study that examined background, knowledge, and attitudes related to the neuroscience of addiction. First, the ABI was distributed as a web-based instrument to a random sample of individuals who teach addiction-specific courses in U.S. colleges/universities (N=358). Second, an in-person survey was administered to undergraduate students enrolled in introductory Criminal Justice, Nursing, and Social Work (N=300) courses at the University of Nevada, Reno (UNR). Data were obtained from a total of 218 addiction educators and 287 students.

**Results:** Addiction educator and student responses were merged for analysis and compared to the eight factors identified by Luke et al. (2002). Factor and item analysis of the merged samples supported six of the Luke et al. (2002) factors (Coping, Efficacy/Inability to Control, Responsibility for Recovery, Genetic Basis, and Moral Weakness), with Cronbach alphas ranging from .62 to .92. Although several items loaded differently in this study than in the original research, they loaded similarly on two component factors (Coping, Efficacy/Inability to Control). Multivariate analysis using the final scale revealed significant addiction attitudes between Addiction Educators and UNR students.

**Conclusions:** Findings from this study suggest that non-treatment individuals may define addiction differently and/or may not share the same constellation of beliefs as those within the addiction treatment field. As such, it is important to consider the target population when developing measures and interpreting results that subsequently guide research-based practices.

**Support:** Funded by the National Institute on Drug Abuse Science Education Drug and Alcohol Partnership Awards # 1 R25 DA 020472-01A1

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### IMPACT OF ADULT ADHD AND COCAINE DEPENDENCE ON MEASURES OF ATTENTION AND IMPULSIVITY.

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**Aims:** Independently, chronic cocaine use and attention deficit disorder (ADHD) have been shown to affect attention and impulsive behaviors. The purpose of this study was to determine if individuals with Adult ADHD and Cocaine Dependence (A+Coc) exhibited greater attention and/or impulsive problems than individuals with Cocaine Dependence alone (Coc) based on their performance on computerized behavioral tasks.

**Methods:** The sample consisted of 53 individuals (91% male; 43% Caucasian; age= 40+/-8). Psychiatric diagnoses were determined by the SCID for DSM-IV and the CAADID [A+Coc (n=17) and Coc (n=35)]. The Immediate and Delayed Memory Task (IMT/DMT) and the GoStop Impulsivity Paradigm (GoStop) were administered to assess focused/sustained attention and impulsive behaviors. The only demographic difference between the two groups was age, the A+C group was significantly younger (t=-2.04, p=.047). There were no differences in recent pattern of cocaine use. Behavioral task analyses were conducted using MANCOVAs covaried for age. For the IMT/DMT we compared 1) % correct detections (CD) (a measure of attention), and 2) % commission errors (CE) and the IMT Ratio (CE/CD) (measures of response initiated impulsivity). For the GoStop we compared response inhibition aspects of impulsivity using the GoStop Ratio (response inhibition failures/responses on go-trials).

**Results:** On the IMT task there were no significant group differences in CDs (F=.18, p=.68), CEs (F=.03, p=.86) or on the IMT Ratio (F=.68, p=.14). On the DMT task there was a trend with the A+Coc group having fewer CDs than the Coc group (63% vs 77%; F=3.56, p=.067). There were no significant differences between the GoStop Ratios.

**Conclusions:** Although these findings did not show any significant differences in immediate attention they suggest that ADHD and cocaine use may create a deficit in sustained attention. Contrary to expectations, individuals with ADHD and cocaine dependence did not exhibit greater impulse control deficits on response initiated or response inhibited behaviors.

**Support:** NIDA grants RO1DA022217 and RO1DA23652

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### PRELIMINARY FINDINGS ON THE EFFICACY OF AN HIV PREVENTION INTERVENTION FOR PREGNANT AFRICAN-AMERICAN WOMEN IN SUBSTANCE ABUSE TREATMENT IN THE SOUTH.

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**Aims:** This study aims to (1) examine the substance use and sex risk behaviors of pregnant African-American women in substance abuse treatment, and (2) determine the efficacy of an adapted evidence-based HIV prevention intervention in reducing risk behaviors.

**Methods:** Pregnant African-American women currently in treatment (N=60) were recruited and randomized into the woman-focused condition, receiving four individual intervention sessions, or into the treatment-as-usual (TAU) condition only. Participants completed a questionnaire about their substance use and sex behaviors via ACASI at baseline and at 3- and 6-month follow-ups.

**Results:** Most participants reported having used alcohol or another substance since they were aware of their pregnancy (77%): tobacco (73%), marijuana (52%), crack (52%), and alcohol (43%). Among participants, 70% had engaged in unprotected sex acts in the past 90 days. Preliminary follow-up data indicate a significantly lower proportion in the woman-focused condition engaged in unprotected sex at 6-month follow-up than at baseline (25% vs. 69%), compared with participants in the TAU condition (56% vs. 69%). Slightly fewer participants in the woman-focused condition had used alcohol, tobacco, marijuana, or crack in the past 90 days at 6-month follow-up than at baseline (92% vs. 94%) compared with the significant decrease for participants in the TAU condition (56% vs. 83%).

**Conclusions:** Pregnant African-American women in substance abuse treatment reported behaviors that pose risk to themselves and their unborn babies. Preliminary evidence indicates that the woman-focused intervention was successful at reducing unprotected sex, but there was little change in the most commonly abused drugs in this sample. This study presents potential intervention barriers and recommendations for future interventions.

**Support:** This research was supported by NIDA grant RO1 DA020852.

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### THE RELATIONSHIP BETWEEN NICOTINE USE AND OPIOID-DEPENDENCE TREATMENT DURING THE EARLY PHASE OF PRIMARY CARE BUPRENORPHINE STABILIZATION.

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**Aims:** Comorbid nicotine and opioid dependence is highly prevalent but understudied. This secondary analysis explores the relationship between nicotine use (**heavy**: >10 cigs/day; **light**: ≤10 cigs/day) and opioid dependence treatment during the first 4 weeks of a primary care buprenorphine/naloxone (BUP/NX) induction study.

**Methods:** Primary dependent measures were treatment retention (Yes/No at week 4) and BUP stabilization, defined as being in treatment, illicit opioid free, and on BUP at week 4. Tobacco use and craving were assessed by self-report, urine cotinine, and the Brief Questionnaire of Smoking Urges (BQSU). Fisher's exact tests were used to explore differences in treatment retention and degrees of BUP stabilization, while paired t tests were used to compare BQSU composite scores.

**Results:** Of 20 participants, 18 (90%) were male, 18 (90%) nicotine dependent, 9 (45%) White, 7 (35%) Hispanic, and 4 (20%) Black. The mean age was 45±11 years. Study retention at week 4 did not differ by smoking status (50%). Average BUP dose was 12.3mg±5.5mg at week 4. One patient quit smoking by week 4. Two of 9 (22%) heavy smokers versus 6 of 11 (55%) light or non-smokers were successfully stabilized on BUP (NS). Average BQSU scores were higher in heavier than light smokers at baseline (6.3±2.6 vs. 3.3±3.6, p=.05) and at week 4 (3.7±2.5 vs. 0.7±1.3, p=.03). Mean BQSU score for smoking individuals stabilized on BUP decreased at week 4 compared to baseline (4.2±3.8 vs. 1.1±1.2, p=.05).

**Conclusions:** Baseline smoking status did not predict treatment retention or BUP stabilization, though sample size may be an important limitation. Cravings were higher for heavier smokers and appear to decrease with BUP stabilization. A better understanding of the interaction between nicotine and opioid dependence may help optimize management of dually dependent individuals initiating BUP treatment.

**Support:** K23 DA020000, K02 DA000465

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### EFFECTS OF PRENATAL STRESS ON LEVER-PRESS ACQUISITION, DELAY DISCOUNTING, AND ETHANOL SELF-ADMINISTRATION IN RATS.

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**Aims:** The prenatally stressed (PS) rat has been found to exhibit altered learning in the presence of aversive stimulation relative to control (CON) rats. It is unclear, however, whether this facilitated learning will occur in the presence of positive reinforcement. In the laboratory, impulsive choice is often studied using a delay-discounting procedure. By using this model, the relation between impulsive choice and other behaviors may be examined. Stress is a major determinant in the acquisition and maintenance of drug taking. There may be a link between stress, altered learning, impulsive choice, and ethanol self-administration. These variables were investigated in a within-subject design.

**Methods:** Differences in response acquisition, delay discounting, and ethanol self-administration were evaluated in PS (n=8) and CON (n = 8) rats. In Experiment 1, differences in lever-press acquisition were evaluated. In Experiment 2, differences in delay discounting were evaluated where choice was between one immediate food pellet (impulsive option) or three delayed food pellets (self-control option). In Experiment 3, a two-bottle choice task was used to determine differences in ethanol self-administration.

**Results:** PS rats obtained significantly more food pellets than CON rats during the lever-press acquisition session. Although the PS rats emitted higher response rates on the operative lever than CON rats, this difference was not statistically significant. Effects of prenatal stress on delay-discounting and ethanol self-administration will also be discussed.

**Conclusions:** PS rats obtained more food pellets in the lever-press acquisition session, which may suggest differences in learning. Examining delay-discounting functions and ethanol self-administration in the PS rat may shed light on directionality of the correlation between drug self-administration, impulsive behavior, and prenatal stress.

**Support:** West Virginia University Eberly College Doctoral Research Program, Department of Psychology Alumni Fund and Hake Fund.

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### STRESS AND CUE INTERACTION IN THE REINSTATEMENT OF COCAINE-SEEKING IN FEMALE RATS.

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**Aims:** Clinical research suggests that gender differences exist in cocaine dependence. However, little evidence exists regarding sex differences in reinstatement behavior following exposure to stress or drug-associated cues, or whether an interaction between stress and drug-associated cues can enhance cocaine-seeking during relapse. Thus, we assessed the effects of footshock and corticotrophin-releasing factor (CRF) on reinstatement of cocaine-seeking in female rats either in the presence or absence of cocaine-associated cues. It was hypothesized that stress reinstatement in females would be exacerbated with respect to males.

**Methods:** Female Sprague-Dawley rats (n=14) lever pressed for IV cocaine (0.5 mg/kg/infusion) paired with a light+tone stimulus for 10 days. Once responding was extinguished in the absence of cocaine reinforcement (7-10 days), the ability of cocaine-paired cues, footshock (0.25, 0.5, or 0.75 mA; 15 min prior to testing, alone or with cues), or CRF (1.0, 1.5, or 2.0 ug, ICV 60 mins before session, alone or with cues) were examined for their ability to reinstate cocaine-seeking behavior.

**Results:** Cues, but not footshock or CRF, significantly increased reinstatement of cocaine-seeking in female rats (p<0.05). However, the combination of footshock or CRF with cues did not result in levels of responding significantly different from cues alone (p>0.05). Interestingly, heterogeneity of responding to stress was evident, in that a small number of female rats (n=5/14) were very responsive to footshock stress or CRF (p<0.05).

**Conclusions:** Female rats seem less responsive to stress-induced reinstatement than males, with only a small number of females displaying reinstatement. Thus, considerations of gender and stress responsivity may have implications in the development of appropriate medications for the amelioration of relapse risk.

**Support:** These studies were conducted in accordance with the Guide for the Care and Use of Laboratory Animals, as adopted and promulgated by the National Institutes of Health. This research was supported by NIH grants RO1 DA21690 and P50 DA16511



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### CONSISTENCY OF SELF-REPORTED DRUG USE AND URINE DRUG SCREENING FOR HOMELESS MEN AND WOMEN IN A COCAINE DEPENDENCE TREATMENT PROGRAM.

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**Aims:** Few studies have compared self-reported cocaine use with urine drug screening (UDS) data during treatment for cocaine dependence. Gender is also an unexplored factor in the accuracy of such self-reports. We examined consistency between the Addiction Severity Index (ASI), on which individuals report the frequency of drug use during the previous 30 days, and UDS data among participants in a randomized controlled trial that examined the effectiveness of contingency management and behavioral day treatment in reduction of cocaine use in homeless individuals.

**Methods:** UDS's were obtained MWF for 6 months, and the ASI was administered at 2 and 6 months into the program. To examine whether UDS data predicted self-report, a linear regression model was constructed in which cocaine use per ASI was regressed against the proportion of cocaine-positive UDS's obtained during the same 30-day period (M2mo=.17, M6mo=.37).

**Results:** This model was significant at 2 [F(1,172)=88.94, R2adj=.34, p<.01] and 6 months [F(1,167)=74.52, R2adj=.30, p<.01]. When gender and the interaction between gender and UDS were added as predictors to these models at month 2 and 6, neither gender nor the interaction was significant (p>.10). However, at month 6, when examining this model at the highest level of cocaine use per UDS (26% of men, 21% of women), a significant gender difference emerged ( $\beta$ =.24, p<.05) where women's self-reported cocaine use was less biased than that of males.

**Conclusions:** Results indicate self-reported cocaine use and toxicology screens are associated, but far from equivalent. Participants exhibited a bias toward under-reporting cocaine use. Although the present study was not powered to detect gender differences in abstinence, results suggest the discrepancy between the two measures of drug use may be greater for men using cocaine later in treatment. Results may have implications for interpreting gender effects in studies utilizing self-reported substance use as an outcome measure.

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### A BRIEF CULTURALLY-SENSITIVE HIV AND HEPATITIS PREVENTION INTERVENTION FOR URBAN AMERICAN INDIANS: DEVELOPMENT AND PRELIMINARY EVALUATION.

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**Aims:** Ethnocultural minorities in bounded geographies may have unique needs with respect to substance abuse and preventive healthcare, but tailored services are seldom available to populations with very small constituencies. A culturally-targeted HIV and hepatitis prevention intervention for urban American Indians was developed using a community participatory research-driven process. Guided by findings that included widespread experiences of cultural loss and community disintegration, a four-session educational intervention on HIV and hepatitis was designed to incorporate American Indian symbols and concepts, cultural enhancement activities, and historical information about selected American Indian groups. Preliminary evaluation indicates that participants (n to date=84) show significant increases in knowledge about HIV and hepatitis at program completion (p<.001) that are sustained through 6 months post-intervention (p<.001 for HIV; p<.01 for hepatitis). Additionally, participants have significant decreases in days of cigarette use (p<.05) and days of illicit drug use other than marijuana at 6 month follow-up (p<.05), with process evaluation suggesting these delayed effects may be attributable to the intervention's facilitated referral component. This project has provided a unique opportunity for conducting social research and service delivery with an otherwise hidden minority population. Future plans include investigation of the relationship between cultural identity, cultural loss, and substance use.

**Conclusions:** Community participatory approaches and research-driven program designs have the potential to yield responsive and acceptable services for small ethnocultural minorities. The preliminary results support the feasibility of the service model, as well as the need for controlled research examining effectiveness.

**Support:** SAMHSA SP-13321.

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### RELATIVE RATES OF PRESCRIPTION OPIOID ABUSE: COMPARISON OF PUBLIC HEALTH DATABASES.

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**Aims:** Interest in the post-marketing surveillance of prescription opioids continues to grow. While these efforts generally use multiple data streams, how these data are related to each other is not well understood. This study examines three, real-time, product-specific datasets that are part of National Addictions Vigilance Intervention & Prevention PROgram (NAVIPPRO™): the ASI-MV® Connect (patient-level data from 360 addiction treatment facilities) and two Web-Informed Services—Geotemporal Real-time Internet-based Intelligence for Drugs (Media-GRIID™; surveillance of over 20,000 news outlets) and Internet Monitoring of web chatter on prescription drugs. We examined relative rates of abuse estimated by these three datasets and compared ASI-MV® Connect data with data from NSDUH, American Association of Poison Control Centers (AAPCC) and DAWNLive! The TEDS dataset was excluded as it provides no opioid-specific information.

**Methods:** ASI-MV® Connect contains 55,341 cases, WISTM contains 2,051,976 online posts, and in Media-GRIID™, 45,185 articles mention prescription opioids. Rates of prescription opioid products and compounds were calculated in each database for overlapping timeframes (July 2007 to October 2008). Spearman rho correlations compared relative rankings of products/compounds.

**Results:** Significant correlations were found between the ASI-MV® Connect data and Internet monitoring mentions (.70) and with media mentions (.67), with Internet monitoring and media correlating .71. Further analyses compared relative rates of these datasets with three publically available datasets, again with high levels of correspondence. ASI-MV® Connect data correlated with AAPCC data at .72, .81 with DAWNLive! mentions ("other" category), and .90 with NSDUH data.

**Conclusions:** This the first study to compare the relative rates of prescription opioids represented in surveillance datasets. Future research will consider time series analyses to examine correspondences across time to further understand which data are leading and which are following indicators.

**Support:** Inflexion, Inc.

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### YOUTH DRUG ABUSE TREATMENT AND PREVENTION NEEDS IN JALISCO, MEXICO.

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**Aims:** To investigate the prevalence and associated factors to drug use and abuse among high-school students.

**Methods:** A multi-stage random sample of high-school students of Jalisco was given a paper-and-pencil survey based upon an adapted version of the Drug Use Screening Inventory (DUSI) developed by Tarter and colleagues (N=24,699; n=2,832). The DUSI showed adequate psychometric characteristics in this population. The statistical analyses accommodate the complex survey design, with attention to unequal probability of selection and clustering of participants within schools and regions.

**Results:** An estimated 44% of the students had smoked tobacco, one of five students was a current smoker, and one of four students used to smoke but had not smoked for a year or more. In contrast, 7.5% of the students reported having used marijuana or cocaine or both. Behavioral problems, deviant peer affiliation, and troubled families were independently associated with drug use. One in two students who used tobacco or alcohol used these drugs in the past year (46% and 54%, respectively), and one in four students who used marijuana or cocaine in their lifetime used these drugs in the past year (28% in both cases).

**Conclusions:** The rates of cocaine use as well as the proportion of current users, were higher than expected and indicate that changing patterns of drug use in Mexico may be creating new treatment needs and complexities. Such a problem can be addressed by the new CAPA (Vida Nueva) Clinics Program from the government among other institutions.

**Support:** University of Guadalajara (Jalisco), CONACYT-SIMORELOS; NCMH grant MD002803, and NIDA International Program, Z as well as NIDA, grants DA12390 & DA19805

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**GENDER AND THE GLOBAL DRUG TRADE: THE CASE OF INCARCERATED WOMEN IN LIMA, PERU.**

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**Aims:** The aim of this research is to understand how women participate in the Peruvian and global drug economy. I will explore how the forces of race, class, gender, and transnationalism intersect in the lives of women prisoners who have been incarcerated in their roles as transporters, sellers, and consumers of drugs, as well as for their association with men in the drug trade. I hypothesize that that social stratification structure of the prison parallels that of the drug trade. One primary theme of this research will be the changing roles of women in the over-all global drug trade.

**Methods:** This paper is based on six months of fieldwork at the Women's Penitentiary Establishment of Chorillos in Lima, Peru. I conducted qualitative interviews with 50 Peruvian and non Peruvian women who were incarcerated for crimes of drug use and drug trafficking.

**Results:** Tentative research results show that prisoners are divided into several categories based on the work they did in the international/local drug trade. Foreign women in the prison who worked as couriers in the international market are at the top of the prison economic hierarchy. The next group is made up of female Peruvian prisoners whose families continue to participate in the drug trade and are therefore able to provide more capital and goods to their incarcerated female relatives than those prisoners whose relatives work low wage jobs. Finally there are the Peruvian prisoners who do not have family or other social networks that provide them with money or goods. These women typically worked at the lowest levels in the drug trade. They compete among one other for the service jobs provided by the prison and wealthier prisoners.

**Conclusions:** This research indicates that the social stratification structure of the drug trade is reproduced in the prison. The roles of women in the drug trade are linked to their social-economic status in the prison. These categories are flexible and a prisoner's status may change. A prisoner's economic position is important because it helps determine how long she will remain incarcerated.

**Support:** BEHAVIORAL SCIENCES TRAINING IN DRUG ABUSE RESEARCH T32DA007233; Public Health Solutions

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**REDUCED FRACTIONAL ANISOTROPY IN HUMAN MDMA USERS IS CONSISTENT WITH CORTICAL AXON LOSS: A 3 TESLA DIFFUSION TENSOR MRI STUDY.**

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**Aims:** MDMA (3,4-methylenedioxymethamphetamine; Ecstasy) remains a widely-used party drug that potentially produces brain serotonin axon loss. Diffusion tensor imaging (DTI) methods assay the diffusion of water molecules and can indirectly measure changes in fiber bundles posing barriers to free diffusion of water. Unrestricted diffusion is isotropic and as diffusion becomes less free (due to structural barriers) the fractional anisotropy (FA) increases. DTI methods have proven sensitive to detecting effects of axon damage, where lower FA indicates loss of axons or myelin.

**Methods:** We recruited 23 MDMA users (age 25±4.9 years) and 23 non-MDMA users (age 22.5±4.6 years) for a DTI study. Subjects underwent DTI using single-shot echo-planar imaging on a Philips 3 Tesla MRI scanner. Data were analyzed using standard methods in SPM5 to compare whole-brain FA between groups. T-maps of between-group contrasts in FA were generated using an extent threshold of 50 voxels and height threshold of  $p < 0.005$  uncorrected for multiple comparisons. Regions having a cluster level uncorrected  $p < 0.05$  were considered significant.

**Results:** MDMA users had used MDMA an average of 28.1±27.4 times (range 3-125 times). In the DTI analysis, MDMA users had lower FA than controls in two brain regions and no areas of increased FA relative to controls: The first was 1.82 cm<sup>3</sup> and included portions of right precuneus white and gray matter and dorsal posterior cingulate gyrus gray matter. The second was 1.13 cm<sup>3</sup> and was located in the left frontal lobe white matter adjacent to the claustrum.

**Conclusions:** These findings are consistent with, but not conclusive for, axon loss in posterior and frontal cortical regions in MDMA users. The observed group differences in FA may be due to pre-existing differences, effects of poly-drug use, or MDMA-induced neurotoxicity. Additional studies using complementary methods and probing cognitive functions mediated by these brain regions seem warranted.

**Support:** NIDA — DA015137, DA020149 and DA00366 to RLC; NCRR — Vanderbilt CTSA UL1 RR024975.

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**HEPATITIS C VIRUS KNOWLEDGE, ATTITUDES, BELIEFS, AND EXPERIENCES IN METHADONE TREATMENT PATIENTS WITH HCV INFECTION.**K M Canfield<sup>1</sup>, Steven L Batki<sup>2,3,1</sup>, E Smyth<sup>1</sup>, R Ploutz-Snyder<sup>4</sup>; <sup>1</sup>Psychiatry, State University of New York Upstate Medical University, Syracuse, NY, <sup>2</sup>Psychiatry, University of California, San Francisco, San Francisco, CA, <sup>3</sup>San Francisco VA Medical Center, San Francisco, CA, <sup>4</sup>NASA, Houston, TX

**Aims:** Methadone treatment (MMT) patients have high rates of HCV infection but low rates of HCV treatment. This study describes HCV knowledge, attitudes, beliefs, and experiences (KABE) in HCV antibody positive MMT patients and assesses the feasibility of treatment engagement when HCV education, HCV RNA testing, and direct access to HCV treatment are provided on-site in the MMT clinic.

**Methods:** Standardized KABE interviews were conducted with 64 HCV-positive MMT patients in a Central New York MMT clinic. An HCV treatment "Contemplation Ladder" was used to assess level of readiness to seek HCV treatment. Participants were offered on-site quantitative HCV RNA testing and the opportunity to participate in a NIDA-funded study offering standard HCV treatment on-site in the MMT clinic.

**Results:** The majority of participants demonstrated adequate knowledge of HCV disease basics, but had poor understanding of HCV tests and treatment. Only 30% reported ever receiving HCV counseling, only 27% reported ever being offered HCV treatment in the past, and only 1 patient had ever started HCV treatment. While over half of participants expressed fear of HCV medication side effects, the majority (78%) expressed willingness to receive HCV treatment and 88% agreed to on-site quantitative HCV RNA testing to confirm chronic HCV infection. Most (79%) of those with confirmed chronic infection chose to enter the HCV treatment study and 50% started HCV medication.

**Conclusions:** HCV-positive MMT patients demonstrated poor understanding of HCV treatment and none were receiving treatment at the time of their interviews. However, most accepted HCV assessment and expressed interest in seeking HCV treatment when provided with on-site HCV education, on-site HCV RNA testing and the opportunity to receive HCV treatment on-site at the MMT clinic.

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**BEHAVIORAL AND MECHANISTIC STUDIES OF THE HALLUCINOGENS DIPT AND 4-OH-DIPT.**

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**Aims:** Commonly abused synthetic hallucinogens N,N-diisopropyltryptamine (DiPT) and 4-hydroxy-N,N-diisopropyltryptamine (4-OH-DiPT) produce different subjective effects (e.g., auditory hallucinations) than other well-known abused hallucinogens. Little is known of these compounds, except that both compounds bind to the 5-HT<sub>2A</sub> receptor, which is the site of action for most classical hallucinogens.

**Methods:** Drug discrimination and electrophysiology were used to investigate potential mechanisms of action. Adult male rats were trained to discriminate between commonly abused compounds and saline using a FR10 schedule of reinforcement. DOM, LSD, and DMT represented the three major classes of hallucinogens, whereas cocaine, methamphetamine, and MDMA represented the psychostimulants. DiPT and 4-OH-DiPT were tested for substitution for each of these drugs. The electrophysiology assay tested for percent inhibition of the mouse wild-type 5-HT<sub>3</sub> receptor in frog oocyte cells.

**Results:** DiPT fully substituted for DMT and DOM and partially substituted for LSD. DiPT did not substitute for methamphetamine, cocaine or MDMA. 4-OH-DiPT fully substituted for LSD and DOM, and partially substituted for cocaine, methamphetamine, MDMA, and DMT. In the electrophysiology assay, both DiPT and 4-OH-DiPT produced significant inhibition of the 5-HT<sub>3</sub> receptor.

**Conclusions:** DiPT and 4-OH-DiPT have discriminative stimulus effects similar to other abused hallucinogens. 4-OH-DiPT may also have some psychostimulant-like effects. Both drugs inhibited the 5-HT<sub>3</sub> receptor, which may contribute to their other subjective effects.

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### ROLE OF ADRENERGIC RECEPTORS IN THE REINSTATEMENT OF EXTINGUISHED COCAINE-INDUCED CONDITIONED PLACE PREFERENCE BY COCAINE, FORCED SWIM STRESS, AND YOHIMBINE IN MICE.

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**Aims:** The responsiveness of central noradrenergic systems to stressors and cocaine poses norepinephrine as a potential common mechanism through which drug re-exposure and stress promote relapse. This study investigated the role of noradrenergic systems in the reinstatement of extinguished cocaine-induced conditioned place preference by cocaine and stress in mice.

**Methods:** Following the establishment of conditioned place preference (15 mg/kg, ip) using an unbiased approach, preference was extinguished by repeated exposure to the conditioning apparatus in the absence of cocaine. The ability of cocaine (15 mg/kg, ip), a physical stressor (forced swim: 6 min, 22-25°C), or the alpha-2 adrenergic receptor antagonist and putative pharmacological stressor, yohimbine (2 mg/kg, ip) to reinstate preference was determined following pretreatment with the beta adrenergic receptor antagonist propranolol (10 mg/kg, ip), the alpha-1 adrenergic receptor antagonist prazosin (2 mg/kg, ip) or the alpha-2 adrenergic receptor agonist clonidine (0.03 mg/kg, ip).

**Results:** Extinguished place preference was re-established by cocaine, yohimbine or forced swim. Propranolol blocked reinstatement by yohimbine, but not cocaine. By contrast, prazosin and, surprisingly, clonidine failed to block reinstatement by yohimbine or cocaine. The effects of adrenergic drug pretreatments on reinstatement by forced swim will be reported.

**Conclusions:** These findings suggest that cocaine-induced reinstatement of place preference does not require adrenergic receptor activation, even though stimulation of central noradrenergic neurotransmission is sufficient to reinstate. Further, the findings question the pharmacological specificity of yohimbine and therefore raise concerns regarding its use to study the mechanisms underlying the involvement of stress and norepinephrine in relapse. Clarification of the involvement of adrenergic receptors in stress-induced relapse awaits determination of the effects of drug pretreatments on reinstatement by forced swim.

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### MALE-FEMALE DIFFERENCES IN TOBACCO DEPENDENCE EXPERIENCES: EPIDEMIOLOGICAL EVIDENCE FROM THE UNITED STATES, 2006.

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**Aims:** We study male-female variations in the experience of tobacco dependence clinical features in an epidemiological sample of community-dwelling United States residents.

**Methods:** Data are from the 2006 National Survey on Drug Use and Health (NSDUH), with a multi-item Nicotine Dependence Syndrome Scale (NDSS) used to assess five domains of tobacco dependence: Smoking Drive (SD), Behavior Priority (BP), Continuous Smoking (CS), Stereotype (S), and Nicotine Tolerance (NT). Male-female differences were analyzed using a generalized linear model and generalized estimating equations (GLM/GEE).

**Results:** Studying 6944 females and 7456 males with recent tobacco smoking, we found no male-female difference in the estimated prevalence of tobacco dependence (males, 41%; females, 41%;  $p=0.65$ ), but two domain scores disclosed different tobacco dependence experiences. Females were more likely to have high SD scale scores, tapped by items on craving and withdrawal ( $p<0.05$ ), while males were more likely to have stereotyped smoking, tapped by items on more fixed patterns of smoking ( $p<0.05$ ).

**Conclusions:** In this extension of research on the 'topography' of smoking, we find somewhat different tobacco dependence experiences for males and females against a background of relevantly similar overall tobacco dependence prevalence. Our next step is research on differential item functioning to assess whether the observed male-female difference might be associated with a measurement bias.

**Support:** NIDA awards R01DA016558, K05DA015799, D43TW05819.

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### ASSESSMENT OF NICOTINE DEPENDENCE AMONG ADOLESCENT SMOKERS: A COMPARISON OF MEASURES.

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**Aims:** Tobacco use often starts in adolescence, yet it is unclear if, when, and how adolescents become nicotine dependent. Assessment of dependence among adolescent smokers is challenging for two primary reasons: 1) patterns of smoking often do not compare to those of adults, and 2) many assessment measures were established first among adults and only later applied to adolescents.

**Methods:** Based within a clinical trial of smoking cessation among adolescents, this study examined the comparative predictive ability of two well-established dependence measures: the Fagerström Test for Nicotine Dependence (FTND) and the Hooked on Nicotine Checklist (HONC). Rather than using self-reports of cigarettes per day as a criterion outcome (which itself is prone to measurement error and is included as one item of the FTND), we report on the relationship between each dependence measure and two objective indices of tobacco exposure: 1) cotinine (gas chromatography), and 2) exhaled carbon monoxide (CO). Eligible participants were adolescents ages 12-21 who smoked >5 cigarettes per day on average, and whose urine cotinine was >100 ng/ml at baseline. Data are based on those who completed each measure and who provided a urine cotinine sample (N=72) or CO (N=83) at baseline.

**Results:** Results showed that the FTND was highly predictive of cotinine ( $p<.001$ ;  $R^2 = .3$ ). However, the HONC was only marginally predictive of cotinine ( $p=.07$ ;  $R^2 = .05$ ). As for expired CO, the FTND was again highly predictive ( $p<.001$ ;  $R^2 = .12$ ), whereas the HONC was not ( $p=.3$ ;  $R^2 = .01$ ).

**Conclusions:** These results are surprising given that the FTND was established among adult smokers and the HONC was created specifically for adolescents. Upon replication, our data provide caution with regard to assessment of nicotine dependence among adolescent smokers.

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### USING LATENT CLASS ANALYSIS TO EXAMINE PATTERNS OF HIV RISK BEHAVIORS AMONG WOMEN WITH LIFETIME HISTORIES OF ILLICIT DRUG USE.

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**Aims:** To examine patterns of HIV risk behaviors among women who use illicit drugs in order to inform HIV prevention interventions.

**Methods:** Two hundred and fifty three women (59.7% African-American, 38.7% White, and 1.6% Other) with lifetime histories of illicit drug use were recruited in Baltimore, Maryland and completed the HIV Risk Behavior Interview and a demographic questionnaire. Five lifetime HIV risk behaviors were examined including early sexual debut, sex trade, having had a casual sex partner, sexually transmitted infection, and injection drug use (IDU).

**Results:** Forty two percent of women reported their sexual debut prior to 15 years of age, 35.9% reported a history of sex trade, 53.6% reported a history of having a casual sex partner; 40.6% reported a sexually transmitted infection, and 60.9% reported injection drug use. The best solution consisted of three classes. The largest class (49.1%) consisted of women with relatively low levels of sexual risk, but high levels of IDU. The second largest class (26.2%) consisted of women with high levels of early sex initiation, history of sex trade, and injection drug use and moderate levels of ever having a casual sex partner or a sexually transmitted infection. The third class (24.7%) consisted of women with relatively low levels of sex trade and IDU, moderate levels of early sex initiation, and high levels of ever having a casual sex partner or sexually transmitted infection.

**Conclusions:** These results suggest varying patterns of HIV risk behavior among drug using women whereby women are at risk for HIV by virtue of either 1) high risk sexual behavior, 2) injection drug use, or 3) both high risk sexual and injection drug use behaviors. These findings underscore the need to tailor HIV prevention interventions to fit the needs of subgroups of drug using women at risk for HIV.

**Support:** This research was supported by grants 2T32DA007292 and R01DA014498 from the National Institute on Drug Abuse (PI: William Latimer, Ph.D., M.P.H.).

**EFFECTS OF NEUROPEPTIDE Y ON THE REINFORCING EFFICACY OF WATER AND COCAINE.**

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**Aims:** To use a progressive ratio (PR) self-administration procedure using water or cocaine reinforcers and, for half the subjects, an explicit negative consequence (shock), to evaluate the effects of neuropeptide Y (NPY) on the reinforcing efficacy of water and cocaine.

**Methods:** Rats were trained on a PR schedule for water (0.3 ml PO) or cocaine (1.5 mg/kg IV) reward. The measure of reinforcing efficacy was the breakpoint (BP) defined as the maximum number of snout pokes a rat was willing to make to receive a reinforcer. Once the rats reached a stable BP over consecutive days of training, two matched groups of rats were formed with equivalent BPs. A 1mA foot shock was then co-administered with each reward in a Punished group while a matched Control group received no shocks. Starting with 0.01 s, the duration of the shock was increased until the BP of the Punished group was reduced to 50-25% of baseline BP. After a new stable BP was reached in the Punished group, each group received escalating doses of NPY (0µg, 0.1µg, 0.3µg, 1µg, and 3µg ICV), with one day off between each microinjection.

**Results:** Increasing the duration of the shock decreased BPs to 50-25% of control levels in both the water and cocaine reinforcer groups. Cumulative record data from individual rats indicated an increase in the post-reinforcement pauses of punished rats. In rats trained with the water reward, NPY increased the breakpoint and decreased the post-reinforcement pauses in the Punished group, but had no effect in the unpunished Control group. The effect of NPY in the cocaine reward group is currently being evaluated.

**Conclusions:** NPY increases the reinforcing efficacy of water reinforcers that are associated with punishment, but does not affect the reinforcing efficacy of water reinforcers that are not associated with punishment. One interpretation of these results is that central administration of NPY reduces the anxiogenic effects of the water/shock combination.

**Support:** Supported by NIH/NIDA DA21261

**NEUROIMAGING OF BRAIN ACTIVATION IN RESPONSE TO FOOD CUES IN OBESE CHILDREN.**

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**Aims:** Childhood obesity is a serious public health problem that has reached epidemic proportions. An addiction model of childhood over-eating behavior predicts that altered reward value and salience of food cues plays a critical role in childhood obesity. The primary aim of this study was to determine if the pattern of regional brain activation to food cues versus non-food cues differs between obese and normal weight children.

**Methods:** Functional MRI at 3.0 Tesla was used to measure differences in food cue-induced regional brain activation in 14 obese and 14 normal weight healthy children ages 8-12. Subjects were studied after a 4-hour fast and following ingestion of a standardized meal. Blood-oxygen-level dependent [BOLD] changes associated with visually displayed food images were contrasted with response to non-food items across fasted and fed conditions in obese and normal weight children.

**Results:** Preliminary analysis of fMRI data in a subset of our pilot subjects (n=8) showed that obese children, compared with normal weight children, have greater activation in response to food cues in reward-related regions of the brain, including the insular region ( $t=3.60$ ;  $p<0.04$ ), the hippocampal region ( $t=3.60$ ;  $p<0.04$ ), and the orbitofrontal cortex ( $t=3.74$ ;  $p<0.04$ ).

**Conclusions:** Obese children show greater activation in reward-related regions than normal weight children when response to food cues are compared to non-food cues. The data is compatible with altered reward value and salience of food cues in obese children. This demonstration of altered reward-related neural activity suggests the relevance of the addiction model in designing methods for prevention and treatment of childhood obesity.

**Support:** NICHD R21 HD053766; NIDA T32 DA021123; NCRR Vanderbilt CTA grant 1 UL1 RR024975.

**ABNORMAL BRAIN METABOLITE LEVELS IN CHILDREN WITH PRENATAL NICOTINE EXPOSURE.**

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**Aims:** Prenatal Nicotine-exposure (NIC) may be associated with abnormal brain development, although the data in humans are limited. This study aims to evaluate whether brain metabolite levels are different in young children (ages 3-4 years) with or without prenatal exposure to NIC.

**Methods:** 48 children (24 NIC, ages  $46.4 \pm 1.7$  months; 24 non-exposed controls, ages  $45.9 \pm 1.3$  months) were evaluated. Each completed detailed clinical assessments, including neuropsychological tests and localized 1H MRS in 4 brain regions (unsedated on a 3 Tesla Siemens Trio MR scanner, PRESS, TR/TE=3000/30ms, 64 averages, 3.5 min per region). LCModel analysis, with water T2 measurements and gray-white segmentation, were performed to determine metabolite concentrations.

**Results:** The two groups had similar height, weight, and head circumference, but the NIC-exposed children showed a trend for lower birth weights ( $p=0.07$ ). Both groups performed similarly on cognitive testing; however, the NIC-exposed children tended to score lower on an Attention task (NEPSY,  $p=0.07$ ). Compared to controls, NIC children had lower total creatine (-6.6%,  $p=0.014$ ) in basal ganglia and higher glutamate in anterior cingulate (10.5%,  $p=0.012$ ). Age-related decline in anterior cingulate choline was observed only in controls ( $r=-0.52$ ), but not in NIC children (Age x NIC exposure:  $p=0.02$ ). Glutamate declined with age in both groups in the anterior cingulate ( $r=-0.31$ ,  $p=0.04$ ) and the frontal white matter ( $r=-0.35$ ,  $p=0.02$ ).

**Conclusions:** NIC-exposed children may have abnormalities in energy metabolism (lower creatine) in the basal ganglia and neuronal metabolism (with higher glutamate) in anterior cingulate. The absence of age-related decline in choline in the anterior cingulate may indicate a delay in cellular reorganization in the NIC-exposed group. Longitudinal follow-up will determine whether these brain metabolite differences affect behavioral outcomes of these children.

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**HIV TRANSMISSION RISK BEHAVIORS AMONG OPIOID-DEPENDENT HIV-INFECTED INDIVIDUALS ENTERING INTEGRATED BUPRENORPHINE AND HIV CARE.**

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**Aims:** We sought to describe factors associated with sexual and injection-related risk behaviors among individuals entering a nationwide demonstration program integrating buprenorphine treatment into HIV care.

**Methods:** We analyzed self-report data on 447 HIV-infected opioid-dependent persons. We conducted bivariate analyses to identify relationships by creating partial least squared or logistic regression models. Odds ratios were calculated to determine demographic, clinical and substance use factors associated with 1) needle sharing and 2) unprotected anal or vaginal sex within the previous 90 days.

**Results:** 42 (9%) participants reported needle sharing. In a multivariable analysis, factors significantly associated with needle sharing included homelessness (OR 4.80; 95%CI: 2.07, 11.10) heroin (OR 4.31; 95%CI: 1.10, 16.87) amphetamine (OR 4.27; 95%CI: 1.26, 14.47) and marijuana (OR 3.19; 95%CI: 1.36, 7.47) use, and Brief Symptom Inventory anxiety trait (OR 2.46; 95%CI: 1.44, 4.20). 106 (24%) participants reported unprotected vaginal or anal sex. Women (OR 1.82; 95%CI: 1.08, 3.05) those reporting living with a partner (OR 3.13; 95%CI: 1.88, 5.21) any alcohol use (OR 1.78; 95%CI: 1.09, 2.93) and amphetamine use (OR 2.98; 95%CI: 1.08, 8.19) were more likely to report unprotected sex. Whites were less likely to report unprotected sex compared to Blacks (OR 0.44; 95%CI: 0.20, 0.93). Those completing high school were less likely to report unprotected sex compared with those who had not (OR 0.53; 95%CI: 0.30, 0.94).

**Conclusions:** Recent HIV transmission risk behaviors are prevalent among HIV-infected persons entering opioid agonist treatment. In addition to buprenorphine, targeted counseling addressing comorbid substance use, social and mental health issues could have important implications for reducing HIV transmission.

**Support:** This initiative is funded by HRSA Grant #H97HA03793.

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### MEMORY FUNCTIONING OF OPIATE-DEPENDENT INDIVIDUALS DURING METHADONE MAINTENANCE TREATMENT WITH COGNITIVE BEHAVIORAL TREATMENT.

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**Aims:** Cognitive Behavioral Treatment (CBT) relies heavily on good cognitive functioning to provide education and skills training to improve decision making, problem solving, planning, and goal setting. CBT also utilizes techniques and materials that engage and depend on memory, understanding, and reasoning. We conducted a study to evaluate changes in cognitive performance of opiate-dependent individuals during methadone maintenance treatment (MMT) combined with CBT during the initial 15 weeks of treatment and investigated the relationships between achievement of good treatment outcomes and improvements in memory functioning.

**Methods:** Memory assessments, including the Rey-Osterrieth Complex Figure (ROCF) test of long-term visual memory, were conducted during the first 3 weeks of treatment and repeated monthly. During the ROCF test, subjects first copied the complex figure and then reproduced it from memory, with delay (36 minutes on average) during which they performed other tasks (computerized and paper-and-pencil assessments). Study participants with less than 50% negative urine toxicology tests for illicit opiates and cocaine during treatment were classified as poor treatment outcomes (n=18), while those with 50% or more negative urine toxicology tests for illicit opiates (and cocaine) were classified as good treatment outcomes (n=17).

**Results:** The study sample included 30 males and 5 females; 20 (57%) were white, 26 (74%) had at least high school education, mean (SD) age was 41 (11). All were HIV negative. MMT patients with good treatment outcomes also achieved significantly greater improvements on their ROCF memory performance over time as compared to patients with poor treatment outcomes during MMT ( $p<0.05$ ).

**Conclusions:** MMT patients who significantly reduce or abstain from illicit drug use also improve their memory/learning/cognitive functioning during MMT with CBT. Achievement of abstinence early in treatment may facilitate the effectiveness of psychosocial interventions, such as CBT, that rely on good cognitive/learning/memory functioning.

**Support:** R01 DA13108 & K24 DA000445

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### MALE- FEMALE VARIATIONS IN CANNABIS SMOKING FOR U.S.-BORN VS. FOREIGN-BORN LATINOS AND ASIANS IN THE UNITED STATES, 2002-2003.

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**Aims:** We use an epidemiological approach to study three hypotheses: (1) US-born Latinos and Asians (LA) are more likely to have smoked cannabis, as compared to foreign-born LA, even with male-female (M-F) differences held constant; (2) the M-F association is expected to be very robust for foreign-born LA; (3) there is no M-F difference in persistence of cannabis smoking once it starts.

**Methods:** Data are from the US National Latino and Asian American Study (NLAAS), designed as a probability sample survey of 4649 household-dwelling adults in 2002-3, with standardized cannabis smoking assessment. Our regression models take survey design and weights into account (STATA 9).

**Results:** As hypothesized, cumulative occurrence of cannabis smoking was greater for US-born Latinos and Asians (50% & 45%, respectively) as compared to foreign-born (16% & 11%, respectively). Among Asian adults, the M-F difference in occurrence of cannabis smoking was null among US-born Asian adults (age-adjusted Asian OR = 1.3,  $p>0.05$ ), but was robust among the foreign-born (OR=2;  $p<0.05$ ). Our hypothesis about M-F variation was not supported for the Latinos: there was robust M-F variation for both US-born and foreign-born (age-adjusted OR = 2.5 and 3.1, respectively;  $p<0.05$ ). Estimates also confirmed our hypotheses about sex and persistence of cannabis smoking among Asians and foreign-born Latinos, but not among US-born Latinos: US-born Latino males were more likely than females to experience persistence of cannabis smoking once it started (OR=2.3;  $p<0.05$ ).

**Conclusions:** We outline three avenues for future research directions that should build upon these empirical estimates, including research on acculturation, assimilation, and acclimatization processes experienced by recent immigrants to the US.

**Support:** NIDA Awards K05DA015799; MSU VPRGS funds.

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### THE EFFECT OF GP120 ON THE ANTINOCICEPTION INDUCED BY OPIOIDS IN THE COLD WATER TAIL-FLICK TEST.

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**Aims:** Cross-desensitization between the receptors for CCL5/RANTES and CCL12/SDF-1 $\alpha$  in the regulation of antinociception has been reported from our laboratory. Because gp120 binds to the same receptor as CCL12/SDF-1 $\alpha$  (CXCR4), the present experiments were designed to investigate the effect of gp120 on the antinociception induced by morphine and the  $\mu$ - and  $\kappa$ -selective opioid receptor agonists, DAMGO and dynorphin, respectively.

**Methods:** Rats were housed individually after surgical implantation of cannulae into the periaqueductal grey (PAG). Experiments began 1 week postoperatively. The cold-water tail-flick test was used as an antinociceptive index. A cutoff time was set at 60 sec. The percent of maximum possible antinociception (MPA%) for each animal at each time was calculated using the following formula: %MPA = [(test latency - baseline latency)/(60 - baseline latency)]  $\times$  100.

**Results:** The results showed that (1) gp120 (50 to 200 ng/ $\mu$ l, PAG) itself has no effect in this range; (2) gp120 (100 or 133 ng/ $\mu$ l, PAG) can dose-dependently reduce the antinociception induced by morphine (100 ng/ $\mu$ l, PAG), DAMGO (400 ng), and dynorphin (20  $\mu$ g/ $\mu$ l, PAG).

**Conclusions:** These results suggest that the gp120 antagonism of antinociception induced by opioids is via CXCR4 expressed in the brain of rats.

**Support:** Supported by NIDA Grants DA 06650 and DA13429

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### TESTING PATHWAYS BETWEEN ALCOHOL AND OPIOID DEPENDENCE.

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**Aims:** Given growing concern about interactions between alcohol and nonmedical opioid use, this study aims to test directionality of the pathways between alcohol and opioid dependence.

**Methods:** Retrospective data from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) were analyzed using survival analysis to estimate time to onset of dependence among 4422 and 131 respondents with alcohol and nonmedical opioid dependence, respectively. Kaplan-Meier curves compared the cumulative incidence and Cox proportional hazards models with time-dependent covariates estimated the risk of one disorder following the onset of the other.

**Results:** Three-quarters (76%) of those with history of opioid dependence also had alcohol dependence compared to 12% of those without opioid dependence. Although the majority of cases of alcohol dependence among those with opioid dependence had an onset prior to age 25 years, nearly one-third had an onset later in adulthood. There was substantially higher occurrence of opioid dependence among those with versus without history of alcohol dependence (2.1% versus 0.1%, respectively). Alcohol abuse alone signaled little increased risk of opioid dependence. Relative hazards of alcohol dependence for those with versus without preexisting opioid dependence was 11.7 (95% CI = 5.4 – 25.1), adjusted for demographic characteristics and other illegal drug dependence. Similarly, preexisting alcohol dependence signaled high risk of opioid dependence (adjusted hazards ratio = 24.5, 95% CI = 9.8 – 61.7).

**Conclusions:** The extremely high prevalence of alcohol use disorders among those with opioid use disorders points to the need for addressing multiple disorders in treatment and suggests opportunities for prevention of secondary disorders. The bi-directional association suggests shared vulnerability, and may have implications for clinical screens identifying candidates for opioid pain management.

**Support:** Support was provided by GlaxoSmithKline and National Institute on Drug Abuse DA020667.

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**COCAINE-ADDICTED INDIVIDUALS WITH PRIOR TRAUMA HAVE A "CUE-SENSITIVE" BRAIN.**

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**Aims:** We recently found that cocaine patients with a prior trauma history (vs. those without) showed markedly greater limbic reactivity to both "seen" and "unseen" aversive cues. In the current analyses, we tested whether prior trauma might also be associated with hyper-responsivity to appetitive (drug and sexual) cues, pointing to a general "cue sensitivity"/ regulatory deficit in addicted individuals with a history of trauma.

**Methods:** We used "fast" event-related BOLD fMRI (functional magnetic resonance imaging) at 3 Tesla to measure the brain response to cocaine-related and to comparison (sexual, aversive and neutral) cues of 33 msec duration in 19 cocaine patients. Each cue (24 stimuli per category) was "backward-masked" by a 467 msec neutral stimulus to prevent conscious recognition. Data were pre-processed within SPM 2, with pre-planned contrasts. Patients were divided into two groups based on trauma history ("Prior Trauma", n=9 vs. "No Prior Trauma", n=10), using a related question from the Addiction Severity Index.

**Results:** Cocaine patients with a prior trauma history showed striking reactivity to "unseen" cocaine cues in limbic regions of interest (e.g., r. amygdala,  $p<.000$  cluster-corrected,  $t=9.05$ ; ant.insula, v. striatum, v.m. prefrontal cortex, ant. cingulate, all  $2>t<10$ ), while patients without a trauma history did not show differential reactivity. Prior-trauma patients also had greatly enhanced limbic reactivity to "unseen" sexual cues ( $2>t<10$ ), relative to cocaine patients with no history of trauma.

**Conclusions:** These data provide the first evidence that prior trauma is associated with a greater limbic brain response not only to "unseen" aversive cues, but also to "unseen" appetitive cues, in cocaine-addicted individuals. Greater "cue-sensitivity" in trauma-exposed individuals offers a potential brain mechanism for relapse vulnerability, and an important treatment target.

**Support:** NIDA (RO1DA10241; R21DA026114, P50; P60), VA VISN 4 MIRECC, DANA Foundation, and Alexander Foundation

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**CIGARETTE SMOKING AND ITS TREATMENT IN PREGNANT, POLYSUBSTANCE-DEPENDENT WOMEN: KNOWLEDGE, ATTITUDES AND PRACTICE OF PATIENTS AND STAFF**

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**Aims:** This study investigated the knowledge, attitudes and practice regarding cigarette smoking and its treatment in pregnant, polysubstance-dependent women.

**Methods:** Consenting patients (N=87) and staff (N=41) at a perinatal substance use treatment center completed anonymous surveys. Completion rates were 64% and 68% for patient and staff groups, respectively.

**Results:** 80% of patients were pregnant and 20% were less than 2 months postpartum. Patients and staff differed significantly in age (mean of 31 years for patients and 35 for staff;  $p=0.023$ ), educational level (high school degree or greater in 59% of patients and 98% of staff;  $p<0.001$ ) and smoking status (any smoking in past 4 weeks by 94% of patients and 25% of staff;  $p<0.001$ ). Proportion of minorities of patients and staff was similar. Among those patients and staff who ever smoked, staff tried to quit twice as often as patients ( $p=0.040$ ), which persisted when controlled for age and educational level ( $p=0.025$ ). Neither patients nor staff demonstrated excellent knowledge of the health risks of smoking. Compared to staff, patients significantly underestimated the risks of smoking on heart attack, wound healing, and low birth weight ( $p=0.003$ , 0.003 and 0.025 respectively). Staff under-rated their patients' desire to quit smoking compared to the patients themselves ( $p=0.028$ ).

**Conclusions:** Although patients and staff had similar levels of knowledge, results suggest that both groups need further education regarding cigarette smoking. High smoking rates suggest the need for improved smoking cessation strategies for both patients and staff. To effectively address cigarette smoking in substance use treatment programs for pregnant women, organizational interventions that focus on changing staff knowledge, attitudes and practice regarding cigarette smoking may first need to be implemented.

**Support:** Supported by DA 023186 and DA12403

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**THE EFFECTS OF MULTIMODAL TREATMENT ON DELAY DISCOUNTING IN OPIOID-DEPENDENT INDIVIDUALS.**

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**Aims:** Discounting of delayed rewards can distinguish addicts from non-addicts and is often considered a measure of impulsivity. However, there has not been a demonstration of a change in the degree of delay discounting resulting from treatment. This study investigates the effect of combining a variety of treatment methods: buprenorphine maintenance, contingency management (CM), community reinforcement approach (CRA), and therapist counseling, on delay discounting in opioid dependent adults. Subjects were asked to make decisions between hypothetical rewards delivered now or in the future. The choice of a smaller more immediate reward rather than a larger more delayed reward increases the discounting rate.

**Methods:** We randomly assigned participants (n=187 at study completion) aged between 18-55 years who met the DSM-IV criteria for opioid dependence into either a computer-delivered CRA with voucher incentives for abstinence, or voucher incentives alone conditions. Participants in both conditions were maintained on buprenorphine, while participants in the CRA condition also had 30 minutes of individual therapy on alternate weeks. Discounting assessments were taken at intake, during treatment, and at follow-up (3- and 6-month post treatment).

**Results:** Across groups, discounting of delayed rewards decreased over the course of treatment for both the \$1,000 and \$10,000 hypothetical money amounts. In addition, the discounting of the \$1,000 amount was significantly greater than the discounting of the \$10,000 amount.

**Conclusions:** These results suggest that multimodal approaches decreases delay discounting in opioid-dependent individuals.

**Support:** RO1 DA012997

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

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**Aims:** The Addiction Research and Treatment Corporation (ARTC), an outpatient opioid treatment program providing onsite primary medical care and HIV-related care for approximately 3,000 predominantly minority adults in New York City has selected and will shortly implement an electronic health information system that integrates counseling, social services, medical services, case management, HIV services, dispensing information, and administrative and fiscal data. Assessment of system performance is being studied.

**Methods:** Five specific aims (quality, productivity, satisfaction, financial performance and risk management) with nine related hypotheses were chosen for study evaluation utilizing a pre and post-implementation research design. Determination was made to combine our in-house dispensing and social services program with eClinicalWorks, which became available through participation of ARTC in a grant obtained by NYC Department of Health and Mental Hygiene. Interfacing these two electronic programs has presented a number of challenges that have been addressed via various in-house field groups that have examined every aspect of the agency's operations and weekly meetings with representatives from the eClinicalWorks vendor and NYC Department of Health and Mental Hygiene. The pre-implementation data collection phase of the study is nearly complete, and data entry and analysis will be completed by February 2009.

**Conclusions:** The results of this detailed program evaluation have the potential to enhance healthcare outcomes and agency cost-effectiveness in substance abuse treatment settings for this unique patient population.

**Support:** The research portion of this project is supported by a NIDA grant (1R01DA022030-03).

**AGE AND ITS RELATIONSHIP WITH CAUSE OF DEATH AMONG OPIATE USERS.**

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**Aims:** This study investigates how age of opioid users is related to causes of death prior to, during, and after opioid maintenance treatment (OMT), and estimates risks of death from various causes in relation to age.

**Methods:** Data on all opiate dependents in Norway (1997-2003) who applied for and/or were accepted for OMT (n=3789) were cross linked with the Norwegian death registry. The total observation time was 10,934 person years. Deaths were classified as overdose, somatic or traumatic causes during analyses. Age effects were investigated by interaction terms between age and treatment status.

**Results:** A total of 213 deaths was recorded. Of 208 cases with known cause of death, 73 % were subject to autopsy. Deaths were due to drug overdose (54%), somatic (32%), and traumatic causes (14%). Age had a differential effect upon risk of death when out of treatment. Younger opioid users were at greater risk of overdose before entering treatment: older users were at greater risk after leaving treatment. In addition older OMT patients were at higher risk of somatic deaths, during OMT.

**Conclusions:** The high rates of overdose prior to and after treatment emphasise the need to provide rapid access to OMT, to retain patients in treatment, and to offer re-enrolment to patients as swiftly as possible. However, the mortality risk was moderated by age, and varied across age strata. Interventions should particularly be attentive towards the young prior to treatment and the older post treatment.

The high prevalence of somatic disorders in opiate users reflected by deaths among older patients due to somatic causes has implications for screening, treatment and referral, and may also lead to increased treatment costs.

**Support:** The data collection was carried out by employees at the University of Oslo in collaboration with the regional OMT centres without external funding. The authors have no financial relationships that related to the topic of this presentation.

**GREATER PSYCHIATRIC SYMPTOMS IN YOUNG MARIJUANA USERS.**

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**Aims:** Marijuana (MJ) is often the first illicit drug used by adolescents and may exacerbate psychiatric disorders. Abnormal stress responses also may be associated with psychiatric disorders. This study aims to determine if marijuana use in adolescence is associated with psychiatric symptoms or stress induced changes in salivary cortisol.

**Methods:** 34 regular MJ users (19±2 years old, 17 male) and 35 controls (18±3 years old, 19 male) were studied. All were screened for medical and psychiatric conditions, including the Symptom Checklist-90R (SCL90) and Brief Psychiatric Rating Scale (BPRS). Saliva samples were taken prior to, immediately following, and 1 hour after the Trier Social Stress test (TSST) and were assayed for cortisol levels by ELISA.

**Results:** MJ users had used since age 14±2 years, smoked 1.6±1.9g/day, 5±2 days/week, for 50±27 months, with lifetime use of 2614±4331 joints, and last used 6±22 days ago. 11 controls had minimal MJ exposure (1±3 lifetime joints). MJ users had more symptoms on 6/12 SCL90 and 9/24 BPRS measures. Cortisol levels were not different between groups; however, SCL90 Interpersonal Sensitivity (IS) correlated with post-stressor cortisol levels in controls (r=0.4, p<0.04) but not in MJ users (r=0.1, p>0.7). On the SCL90, greater lifetime joints were associated with (r>0.35, p<0.05) higher t-scores on IS, phobic anxiety, paranoid ideation, and general symptom index (GSI), while shorter duration of abstinence was associated with (r<-0.35, p<0.05) higher t-scores on obsessive compulsive, IS, positive symptom total, and GSI.

**Conclusions:** MJ users had more psychiatric symptoms, especially those with more MJ use. Adolescents who used MJ may have altered social stress responses since high IS scores were associated with greater cortisol responses to the TSST only in the controls, suggesting a blunted cortisol response in MJ users. A larger sample and follow-up are needed to evaluate the progression of symptoms, and whether some of these MJ users will develop Axis 1 psychiatric disorders.

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**AGE EFFECTS ON HEROIN AND PRESCRIPTION OPIOID ABUSE AMONG ENROLLEES INTO METHADONE MAINTENANCE TREATMENT.**

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**Aims:** To examine the effect of age on recent heroin and prescription opioid (PO) abuse among enrollees into methadone maintenance treatment (MMT).

**Methods:** A national survey was conducted among 21,748 patients enrolling in 75 MMT programs. Separate logistic regression models for past month heroin and PO abuse were constructed. A cubic polynomial term for age was included after entering covariates for several demographic variables. Two-way interactions between age and race, region, and urbanicity were considered.

**Results:** Mean age was 35 (SD=10.7), 76% were white, 38% female, 60% living in counties with > 1M residents, 58% were heroin users and 70% were PO abusers. Prior to adding the covariates visual analysis indicated that heroin use was higher among 17 to 20 year olds (56%) than among 21 to 25 year olds (48%), especially among whites, and that there was a linear increase in heroin use with age for respondents > 25 years old. Two-way interaction effects between the cubic polynomial for age and the 3 demographic variables indicated little evidence of age effects on heroin use among respondents in the Northeast. The most consistent age effects among heroin users were middle-aged respondents (31 to 60), where the probability of use increased with age among non-white Midwest and West participants and among white Midwest participants. Among PO abusers there was a decrease in POs with age. The most consistent age effects, among PO abusers, were in the middle-aged group, where the probability of use decreased with age among non-urban participants in all four regions and among urban Midwest participants.

**Conclusions:** Non-linear and linear age effects on heroin and PO abuse appear to vary by demographic factors such as race, region and urbanicity.

**Support:** This study was funded by the Research Abuse, Diversion and Addiction-Related Surveillance (RADARS@)

System through a subcontract with the American Association for the Treatment of Opioid Dependence (AATOD).

**ALCOHOL DEPENDENCE AND POST TRAUMATIC STRESS DISORDER: CRAVING AND ALCOHOL-RELATED PHYSIOLOGICAL REACTIVITY TO TRAUMA AND ALCOHOL CUES.**

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**Aims:** Using a cue reactivity paradigm, this study examined the impact of personalized trauma-image cues and in vivo alcohol cues on alcohol-related responding (i.e., salivation and craving) in AD-PTSD subjects. To date, no studies have reported alcohol-related physiological responding to trauma cues. It was hypothesized that subjects would report greater alcohol craving and salivary responding when presented with an alcohol cue compared to a neutral cue. In addition, it was hypothesized that subjects would report greater alcohol craving and salivation upon presentation of a trauma cue when compared to a neutral cue and would evidence the greatest responding when presented with a trauma cue combined with an alcohol cue.

**Methods:** 15 AD subjects with current PTSD were presented with 4 counter-balanced trials consisting of a personalized trauma or neutral narrative and either an alcohol or neutral (i.e., water) cue (i.e., trauma-alcohol, trauma-neutral, neutral-alcohol, neutral-neutral). Salivation, collected via 3 dental rolls inserted in the mouth, was measured during each trial. Alcohol craving and subjective distress were collected following the presentation of each cue combination. Data collection is ongoing.

**Results:** Analyses reveal that subjects exhibited increased distress, F(3,12)=14.99, p<.001, alcohol craving, F(3,12)=56.06, p<.001, and salivary responding, F(3,12)=3.78, p<.05, to trauma and alcohol cues when compared to neutral cues and the combined trauma-alcohol cue elicited the greatest reactivity.

**Conclusions:** Evidence that AD-PTSD subjects exhibit increased alcohol craving and physiological reactivity in response to trauma memories is offered as a potential contributing factor in the poorer alcohol treatment outcomes previously documented in this comorbid population. Given the likelihood that salivary responses to trauma cues are classically conditioned, exposure-based interventions may prove useful in treating this population.

**Support:** NIAAA grant R01AA016816

### VICTIMIZATION, MENTAL DISTRESS, CRIME, AND SUBSTANCE USE AMONG PREGNANT ADOLESCENT GIRLS.

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**Aims:** The aims of this study are to compare adolescent girls who have ever been pregnant with those who have never been pregnant in terms of reported rates of victimization, mental distress, crime, and substance use, and within the pregnant sample, to determine if level of victimization is associated with mental distress, crime and violence, and substance use.

**Methods:** Data are from 70 substance abuse treatment facilities across the United States that utilize 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 4,190 female adolescents (ages 12-17 years) with known pregnancy status, of whom 618 reported having ever been pregnant.

**Results:** Adolescents who have ever been pregnant were significantly more likely than adolescents who have never been pregnant to report high levels of victimization (69% vs. 50%; OR = 2.23, 95% CI=1.85-2.67), externalizing disorders in the form of conduct disorder symptoms (18% vs. 10%; OR=1.98, 95% CI=1.57-2.49), internalizing disorders (25% vs. 15%; OR=1.89, 95% CI=1.54-2.32), past-year substance problems (43% vs. 34%; OR=1.46, 95% CI=1.23-1.74), and crime and violence (50% vs. 41%; OR=1.44, 95% CI=1.21-1.71).

Within the pregnant sample, individuals reporting high victimization were significantly more likely than those reporting low victimization to report high rates of internalizing disorders (26% vs. 3%; OR=11.36, 95% CI=8.1-15.93), externalizing disorders (34% vs. 9%; OR=5.21, 95% CI=4.2-6.46), past-year substance problems (47% vs. 20%; OR=3.09, 95% CI=2.67-3.59), and involvement with crime and violence (55% vs. 23%; OR=4.09, 95% CI=3.53-4.75).

**Conclusions:** These results speak to the importance of screening for victimization and mental distress (internalizing and externalizing disorders) among pregnant adolescents entering substance abuse treatment, so that appropriate intervention may occur.

**Support:** This research is supported by Center for Substance Abuse Treatment Contract No. 270-07-019.

### BEHAVIORAL SENSITIZATION TO COCAINE IN RATS: EVIDENCE FOR TEMPORAL DIFFERENCES IN DOPAMINE D3 AND D2 RECEPTOR SENSITIVITY.

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**Aims:** A growing number of studies in rats, monkeys, and humans have reported decreases in D2 receptor availability following cocaine (COC) administration, however, it is less clear how COC affects D3 receptors. These studies were aimed at evaluating changes in D2- and D3-mediated behavioral effects and receptor expression following COC administration in the rat.

**Methods:** COC (15 mg/kg X 2d; 30 mg/kg X 5d), or saline was administered once daily for period of 7-days (n=24/group). Pramipexole-induced (PRAM; 0.01-1.0 mg/kg) yawning (n=8/group), hypothermia, and locomotor activity (n=6/group) were assessed using a multiple-dosing procedure at 24h, 72h, 10d, 21d, and 42d (yawning only) after COC administration. In vitro binding analyses were performed with 3H-7-OH-DPAT (D3) and 3H-Spiperone (D2) using membranes (ventral striatum) prepared from brains collected at 24h and 42d (n=5/group/time).

**Results:** COC administration produced a leftward and upward shift in the ascending limb of PRAM-induced yawning with significant increases in yawning (0.032 PRAM) observed at 10d (p<0.05), 21d (p<0.001), and 42d (p<0.001), as compared to saline controls. A significant decrease in yawning (0.1 PRAM) was observed in the COC rats at 42d compared to 24h. COC administration also decreased D2 Bmax (p<0.05) and Kd (p<0.001) and increased D3 Bmax (p<0.001) at 42d. COC did not alter PRAM-induced hypothermia or locomotor activity.

**Conclusions:** Convergent evidence from the behavioral and binding studies suggest that COC has differential effects on D3 and D2 receptors. Although COC produced a sustained enhancement of PRAM's D3-mediated effects as early as 10d after COC, changes in D2-mediated effects were not observed until 42d after COC. These findings highlight the need to consider changes in D3 receptor function when thinking about the behavioral sequelae that accompany cocaine abuse.

**Support:** Research supported by F013771, DA020669, HD02528, and NCRRI-NBRE RR016475

### SUSTAINED ATTENTION IS RELATED TO TREATMENT OUTCOMES FOR ADOLESCENT CIGARETTE SMOKERS.

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**Aims:** Sustained attention is often considered a form of impulsive behavior, which has been identified as an independent subfactor of impulsivity using both laboratory behavioral (Reynolds et al., 2008) and self-report (Patton et al., 1995) assessments. Little research has specifically explored relations between inattention and drug-use treatment outcomes. The current study explored associations between sustained attention and smoking-treatment outcomes for adolescents participating in a social-cognitive treatment program (i.e., Not-On-Tobacco).

**Methods:** Eighty-One participants (46 females) attended a pre-treatment laboratory session within two weeks of treatment onset. Participants completed the Conners' Continuous Performance Test II (CPT II) and the Barratt Impulsiveness Scale-11-Adolescent (BIS-11-A). The CPT II is an assessment of sustained attention. Participants were grouped based on treatment outcomes: "reducers" (n = 17; 11 females) reduced self-reported cigarette use by at least 50% and reduced in urinary cotinine levels from pre- to post-treatment assessments; "non-reducers" (n = 39; 20 females) completed treatment but did not reduce their cotinine levels; "dropouts" (n = 25; 15 females) quit the treatment program before its completion.

**Results:** Results showed there were no significant group differences on measured demographic variables (including IQ) or impulsivity based on the BIS-11-A. However, there was a significant group difference for CPT II omissions [F(2, 80) = 3.4, p = .040]. The "reducers" committed significantly fewer CPT omissions (indicating better attention) than the other two outcome groups. The "non-reducers" and "dropouts" did not differ significantly on omissions.

**Conclusions:** These results indicate that ability to sustain attention is related to treatment outcomes for adolescent smokers attempting to quit or reduce smoking during a social-cognitive type program. These findings may indicate treatment modifications to improve treatment outcomes for adolescent smokers who are less able to sustain attention.

**Support:** NIDA R01 DA0203087-01A2

### ABUSE LIABILITY OF IV BUPRENORPHINE VS BUPRENORPHINE-NALOXONE IN BUPRENORPHINE-DEPENDENT INDIVIDUALS.

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**Aims:** Sublingual buprenorphine (BPN; Subutex®) has been used successfully for maintenance treatment of opioid dependence. However, illicit use of BPN does occur. To decrease BPN misuse, a buprenorphine-naloxone formulation (BNX; Suboxone®) was developed. When used intravenously (IV), the naloxone in BNX theoretically precipitates withdrawal in opioid-dependent individuals and blunts the euphoric effects of buprenorphine. The abuse potential of IV BNX in BPN-dependent individuals is unclear given the unique pharmacology of BPN (namely, its slow dissociation from opioid receptors). The present study was designed to assess the abuse potential of IV BPN compared with BNX in BPN-maintained participants.

**Methods:** Heroin-dependent volunteers (N=12) who were willing to inject BPN participated in this randomized, placebo-controlled, double-blind study. Participants were maintained on 2, 8, and 24 mg sublingual BPN for two weeks at each dose. During a morning sample session, participants received \$20 and an IV dose of the test drug (low- or high-dose BPN or BNX, placebo, naloxone, or heroin). During an afternoon choice session, participants were given the opportunity to work for the test drug or money they sampled during the morning session. Each participant received all of the BPN maintenance doses and all of the IV test doses.

**Results:** Self-administration of the BNX combination was lower than that of BPN or heroin (all P=0.0001). Subjective ratings of drug liking and desire to take the drug again were lower for BNX than BPN (P=0.0001). Participants also reported that they would pay less money for BNX compared to BPN (P=0.0001) or heroin (P=0.0001). Opioid withdrawal symptoms were increased by naloxone, but not BNX.

**Conclusions:** When administered IV, the BNX combination was not as well liked and was self-administered less than BPN alone or heroin. This study provides support for the reduced abuse liability of BNX compared to BPN and heroin in BPN-maintained injectors.

**Support:** Supported by Schering-Plough Corp.



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**RESEARCH OPPORTUNITIES IN NIDA'S DIVISION OF EPIDEMIOLOGY, SERVICES AND PREVENTION RESEARCH.**

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**Aims:** DESPR supports integrated scientific approaches to understanding and addressing interactions between individuals and environments that contribute to the continuum of problems related to drug use and addiction.

**Conclusions:** DESPR has identified 3 key research questions: What new theories inform epidemiology, services and prevention research? What intrapersonal and environmental factors interact with each other and with genetic factors across development? How can blending of science and services measurably impact public health outcomes? Within "new theories" are translation studies which link public health and neuroscience, economic and organization/management studies of systems of care, and studies of novel ways to measure the severity of drug addiction. Within "interactions" are studies of how the social environment modifies individual trajectories and treatment responses, as well as a large gene-environment-development program. Finally, "blending" includes studies of drug abuse prevention and treatment services within medical settings (e.g. screening and brief interventions, or studies targeting the emergent problem of prescription drug abuse), and studies of novel approaches to implementing services on a widespread basis. Key cross-cutting themes for DESPR include studies of: a) the HIV-drug abuse nexus with attention to translating research into practice and policy, b) drug abuse and crime, both through research on intersecting crime and drug abuse trajectories as well as prevention and treatment services work, c) studies of the interplay of psychiatric illnesses and drug use disorders (comorbidity) regarding opportunities for novel prevention and treatment service delivery systems of care, and d) health disparities studies to interrupt the way that drug abuse and addiction includes an over-representation of vulnerable populations. The ultimate goal of DESPR is to promote extraordinary public health research to end drug abuse through the work of its Epidemiology, Services and Prevention Research Branches.

**Support:** Fully funded by NIDA.

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**INVOLVEMENT OF THE HYPOCRETIN SYSTEM IN THE REINFORCING EFFECTS OF NICOTINE IN RATS.**

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**Aims:** The neuropeptide hypocretin (hcrt) has recently been implicated in the dependence-related behavioral effects of cocaine and morphine. Noncontingent nicotine administration has also been shown to activate hcrt neurons and upregulate hcrt and its receptors in rat LH. The present study examined whether antagonism of hcrt-1 receptors attenuates nicotine self-administration, and whether a history of nicotine self-administration modulates expression of hcrt and its receptors in several brain areas.

**Methods:** In Experiment 1, rats were trained to self-administer nicotine or respond for food under a fixed-ratio (FR) 5 schedule during 1-hr sessions. Rats were subsequently pretreated with the hcrt-1 receptor antagonist SB-334867 (10, 18, 30 mg/kg). In Experiment 2, rats self-administered nicotine or saline under an FR 1 schedule for 19 sessions and were then sacrificed 5-hr post session to collect tissue from several brain regions, including the rostral and caudal LH, VTA, NAcc, PPTg, PFC, and ARC. Correlations between measures of nicotine self-administration and expression of hcrt and/or its receptor subtypes were examined.

**Results:** In Experiment 1, SB-334867 produced a dose-dependent reduction in nicotine self-administration, but had no effect on food-maintained responding. In Experiment 2, expression of hcrt-1 receptors in ARC was significantly higher in rats that had self-administered nicotine. Although overall expression of hcrt and its receptors in all other areas was not affected by nicotine exposure, mean rates of active lever pressing in the nicotine, but not saline, rats were significantly positively correlated with individual differences in expression of hcrt-2 receptors in cLH and PPTg.

**Conclusions:** The present findings suggest a role for hcrt mechanisms in nicotine reinforcement, and that hcrt signaling within the cLH, PPTg, and ARC may be particularly important.

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**RELATIVE REINFORCING EFFECTS OF OXYCODONE AND MORPHINE IN HEROIN-DEPENDENT VOLUNTEERS.**

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**Aims:** Recent studies have suggested that oral oxycodone (O) and morphine (M) may have different abuse liability profiles based on subjective responses. The purpose of the present study was to examine the relative reinforcing effects of oral O and M.

**Methods:** Heroin-dependent volunteers (N=12) lived in the hospital during this 8-week randomized, double-blind, placebo-controlled study. Participants were maintained on 4 mg sublingual buprenorphine throughout the study. Two different self-administration procedures were used: a drug versus money choice procedure was used during the first test week and a drug versus drug choice procedure was used during the next six test weeks. When participants chose between drug and money, they received \$20 and an oral dose of drug (0, 45, 135 mg M, or 15, 45 mg O) during a morning sample session. Several hours later, participants worked for fractions of the test drug or money that they sampled during the morning session. When participants chose between two doses of drug, they sampled one dose on Mon (Dose A) and a second dose on Tues (Dose B). On Wed-Fri, participants had six opportunities to choose to receive Dose A or Dose B. Drug choices were between placebo and active drug (0 vs 135 mg M; 0 vs 45 mg O), high and low doses (45 vs 135 mg M; 15 vs 45 mg O), low dose M and O (45 mg M vs 15 mg O) and high dose M and O (135 mg M and 45 mg O).

**Results:** When given a choice between drug and money, 18.3 and 11.7% of the low doses of M and O were chosen respectively, whereas 28.3 and 42.5% of the high doses of M and O were chosen respectively. Using a drug versus drug procedure, both M and O were chosen over placebo ( $P < 0.0001$ ) and high doses were chosen over low doses ( $P < 0.0001$ ). A preference between the two low doses of O and M was not detected. However, when given a choice between the high doses of M and O, subjects preferred O over M ( $P < 0.01$ ).

**Conclusions:** Although both M and O have reinforcing effects, O is preferred over M when a drug versus drug choice procedure is used.

**Support:** Supported by DA09236.

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**INTERVENTIONS TO REDUCE HIV RISK AND DRUG USE AMONG HETEROSEXUAL METHAMPHETAMINE USERS: PRELIMINARY RESULTS FROM A PILOT STUDY.**

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**Aims:** This paper reports on the results of a pilot study which examined the feasibility of implementing contingency management among out-of-treatment, heterosexual methamphetamine (meth) users and the likelihood of reducing drug use and HIV risk among this population.

**Methods:** Fifty-eight heterosexual meth users were recruited through street outreach in Denver from November 2006 through March 2007. Subjects were randomly assigned to either contingency management (CM; n=29); or CM plus strengths-based case management (CM/SBCM; n=29) for 17 weeks. Participants were followed at 4 and 8 months. Participants were primarily White (90%), 52% male and averaged 38 years old. Eighty-two percent attended at least one CM session, with 29% of those attending at least fifteen.

**Results:** All participants reduced meth use significantly at 4- and 8-months. Post hoc analyses showed that those who attended more sessions submitted more stimulant-free urines than those who attended fewer or no sessions. Participants assigned to CM/SBCM attended more sessions and earned more vouchers than clients in CM, although differences were not statistically significant. Similarly, participants reported significantly reduced sharing of needles at 4 months and significantly reduced sex under the influence of meth at 8 months.

**Conclusions:** Findings demonstrate that CM and SBCM, alone and in combination are feasible and efficacious for helping out-of-treatment meth users reduce drug use and some HIV risk behaviors. Findings also provide support for conducting adequately powered controlled trials to evaluate the use of CM and SBCM for optimizing meth use and HIV risk behavior outcomes in this population.

**Support:** This study was supported by the National Institute on Drug Abuse, DA 021522-02.

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### DOPAMINE AND SEROTONIN TRANSPORTER AVAILABILITY DURING ACUTE ALCOHOL WITHDRAWAL: EFFECTS OF COMORBID TOBACCO SMOKING.

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**Aims:** Tobacco smoking is highly comorbid with heavy alcohol drinking, yet the interactions of tobacco smoking and alcohol drinking on brain catecholaminergic synaptic markers is unexplored. Here we evaluate the effects of alcohol drinking alone from comorbid alcohol drinking and tobacco smoking on dopamine (DA) and serotonin (5-HT) transporter availability.

**Methods:** 14 heavy alcohol drinking smokers (n=6) and nonsmokers (n=8) and 14 age-matched control smokers (n=6) and nonsmokers (n=8) were imaged with [123I]β-CIT SPECT. Alcohol drinking smokers and nonsmokers consumed 134±100 and 197±140 drinks, respectively over the previous month and were imaged during acute withdrawal (within 5 days of their last drink).

**Results:** DA and 5-HT transporter availability was significantly higher in drinkers compared to controls. However, this elevation was restricted to alcohol drinking nonsmokers, with higher DA transporter availability in the striatum (26%, P=0.003), and higher 5-HT transporter availability in the diencephalon (26%, P=0.02) and brainstem (42%, P<.0001) compared to control nonsmokers. There was no significant difference in DA or 5-HT transporter availability between drinker and control smokers. There was a significant positive correlation between days since last drink and 5-HT transporter availability in the diencephalon (r=0.60, P=0.023) and brainstem (r=0.54, P=0.047), in the total group of alcohol drinkers and in alcohol drinking nonsmokers.

**Conclusions:** During the first week of abstinence, DA and 5-HT transporter availability is higher in alcohol drinking nonsmokers but not alcohol drinking smokers. Smoking may suppress neuroadaptive changes in DA and 5-HT transporters during acute alcohol withdrawal.

**Support:** Department of Veterans Affairs, U.S. Veterans Affairs VISN 1 Mental Illness Research Education and Clinical Center (MIRECC), NIAAA(KO1AA00288; RO1 AA-11321; KO5 AA-14906-01; I-P50 AA-12870-03), NIDA (KO1DA02065; KO2DA21863)

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### CHARACTERISTICS AND NINE-MONTH OUTCOMES OF DISCHARGED METHADONE MAINTENANCE CLIENTS.

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**Aims:** The dropout rate from methadone maintenance treatment (MMT) is high. Moreover, those who drop out of treatment are likely to quickly relapse to opiate use. While some individuals who are discharged from MMT return to treatment, others remain out of treatment placing them at risk for HIV and other diseases. Although much research has examined predictors of retention in MMT, few studies have assessed the characteristics and long-term outcomes of discharged methadone clients.

**Methods:** A total of 230 methadone patients were interviewed three months and then again at nine months following discharge from a VA (43%) and two community-based (57%) MMTPs.

**Results:** The sample was predominately male (82%) with an average age of 44 years and about half were African American (51%) and 45% were Caucasian. They reported an average of 18 years of heroin use. At three months post-discharge, a total of 128 (56%) were not enrolled, but in need of treatment, whereas, 102 (44%) had successfully re-enrolled in treatment. Those who had successfully re-engaged were more likely to be female, not married, unemployed, had a longer history of benzodiazepine use, reported more psychiatric hospitalizations and were originally enrolled in a community-based MMTP rather than a VA facility. Not surprisingly, those who had not re-engaged in treatment reported more recent heroin, cocaine, alcohol, and IV drug use as well as more criminal behavior. In addition to assessing the characteristics of discharged methadone clients, analyses will also examine the nine-month post-discharge outcomes among three groups: 1) those who re-engaged in treatment on their own at three months, 2) those who were provided a case management intervention to assist with treatment re-entry, and 3) those who were provided with a passive referral to MMT.

**Conclusions:** Since MMT is associated with reduced drug use, HIV, and crime, as well as improved employment and mortality outcomes, the findings will highlight the importance of rapid treatment re-engagement.

**Support:** Supported by NIDA and VA grants.

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### CHAOS: THE ROOT OF THE PROBLEM FOR FEMALE CRACK USERS.

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**Aims:** Though chaos has been associated with medical and psychiatric conditions, treatment no shows, and treatment non-compliance, its effect on drug use, or HIV intervention success has been ignored. Investigators at EPRG have been developing and testing a measure of chaos among 501 predominantly African American female crack cocaine users from a NIDA funded study.

**Methods:** Chaos was described by perpetrated emotional, sexual or physical violence or victimization either early or later in life; use of illicit substances before age 15; promiscuity; gun access; childbirth before age 19, number of life events, and other circumstances.

**Results:** Over half of the women (55%) scored high on chaos; high chaos was associated with DSM IV cocaine dependence (63% vs. 45%), PTSD (41% vs. 22%), major depressive episode (45% vs. 26%) and sex trading (66% vs. 45%). In this study, although higher chaos scores were more likely to be associated with cocaine use at each follow-up, they were not associated with either additional recruitment or retention efforts at a 4 and 12 month follow-up. In fact, response rates averaged 94% for both. Lastly, women characterized with low chaos scores who received the highest level of intervention reported the fewest number of crack days over the 12 months of follow-up. Women with the high chaos scores sustained their reduced number of crack days over time.

**Conclusions:** A scale to measure level of chaos can predict response over time. Tailoring interventions to level of chaos could improve outcomes in high risk populations.

**Support:** This work was supported by NIDA R01 DA11622, PI Cottler.

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### BEHAVIORAL INHIBITION IS PREDICTED BY SELF-REPORT MEASURES OF DRUG INTOXICATION AND WITHDRAWAL IN METHAMPHETAMINE-DEPENDENT PEOPLE.

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**Aims:** Methamphetamine (MA) dependent individuals have well-documented neurocognitive deficits including poor inhibitory control, which may contribute to continued use and relapse. It is unknown if an agonist therapy would improve these deficits. We tested whether the potential agonist replacement dextroamphetamine (d-AMP) would improve response inhibition in MA-dependent individuals.

**Methods:** A computerized neurocognitive battery was administered 4 hours after participants' first treatment of either d-AMP (60 mg, N = 30) or placebo (N=30). Response inhibition was measured with a Go/NoGo test. Drug intoxication and withdrawal were measured using visual analog [e.g., high] and Likert-scale [e.g., Amphetamine Withdrawal (AWQ)] questionnaires. We hypothesized that d-AMP would improve Go/NoGo performance and that self-report measures would correlate with Go/NoGo performance.

**Results:** Data are available for 48 of 60 participants in this ongoing study. 90% tested positive for MA in a pre-dose urine test. Dosing condition did not significantly affect Go/NoGo inhibition or baseline-corrected self-report measures. However, Go/NoGo performance was predicted by self-report measures (both baseline and post-dose) of intoxication and withdrawal [e.g. visual analog 'high' (F(1,46)=6.50, p=0.014); AWQ 'hyperarousal' (F(1,46)=5.34, p=0.025)]. Higher self-report intoxication predicted worse performance. Higher withdrawal predicted better performance.

**Conclusions:** First administration of d-AMP did not significantly affect either self-report measures or behavioral inhibition in MA-dependent users. This was likely due to variability in participants' use of MA, which was usually recent. Those reporting either higher intoxication or lower withdrawal had impaired inhibition. If agonist therapy improves impulsivity in MA users, it may interact with self-administered MA in those who relapse.

**Support:** DA018179

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**CRIMINALIZATION OF ADDICTION AND MENTAL ILLNESS: DO NOT PASS GO, GO DIRECTLY TO JAIL.**

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**Aims:** The Missouri Department of Corrections estimates that 75% of its offender population requires treatment for addiction. When offenders are released from prison or jail, they are in need of both mental health and addiction services. These analyses aim to describe the overlap of mental health and addiction services among a high risk population.

**Methods:** Data from St. Louis show significant overlap between high utilizers of mental health and addiction services and the criminal justice system.

**Results:** Specifically, of the top 50 utilizers of mental health and addiction services in St. Louis, over 90% had a prior criminal history, >50% were actively wanted for a crime with over 135 active warrants. Of those 50, 19 had been incarcerated in 2007, with an average of 37 days in jail. Of those, 46% were diagnosed with a substance use disorder, 46% with schizophrenia, 22% with schizoaffective disorder, 36% with a mood disorder, 14% with a personality disorders, and 4% with an anxiety disorder. Nearly half, 48%, had co-occurring mental illness and addiction. In 2007, these top 50 utilizers spent a total of \$3,468,000 in medical services, averaging \$69,374 each. This compares with an average cost of \$27,000 among other utilizers.

**Conclusions:** This work has implications for the mental health, substance abuse and criminal justice communities. While the mental health and substance abuse systems work to reduce time in emergency departments and inpatient treatment, the criminal justice system works to reduce recidivism, increase mental health hospitalization and treatment. Strategies to further evaluate the overall resource utilization of this population, along with structured interventions to reduce risk are critical to the public health and safety. Suggestions for how systems can work better together will be presented.

**Support:** T32 DA07313 (Cottler, PI)

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**RISE IN METH USE IN THE LATINO COMMUNITY.**

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**Aims:** The aim of this research was to investigate the changes in primary drug reported by Latinos entering county funded alcohol and drug treatment programs and to determine what difference exists between the "older" heroin using population and the more recent treatment admissions which report methamphetamine as the primary substance. It was expected that in addition to characteristic differences (mean age, education, and employment) that there were drug use differences (age at first use, frequency of use, route of administration).

**Methods:** Admission and discharge related information was collected from 500 treatment programs. Each record includes the admission date, demographics of the treatment participant, discharge date, and information concerning drug and alcohol use. Additional information was gathered on education, employment, medical/psychological health and treatment, and social relationships.

**Results:** A massive increase in primary meth use by the Latino community and a corresponding decrease in primary heroin use was found from 2001-2008. Primary meth users were younger, better educated, and began using meth at an earlier age than those who reported heroin as the primary drug. In addition, primary meth users also reported shorter average lengths of stay in treatment. Primary heroin users were more likely to report injecting heroin as compared to primary meth users, however, a significant number of primary meth users reported injection behaviors.

**Conclusions:** These results indicate that different treatment methods would be useful in dealing with the influx of Latinos who report using methamphetamine. Currently few protocols exist that deal with methamphetamine use, however the utility of these protocols with the Latino population remains to be seen. Additional areas of concern include the increase shown in injection as a route of administration for primary meth users. Such increases can lead to additional public health concerns (e.g. hepatitis C, HIV, etc.).

**Support:** Crèveœur, D. A., Finnerty, B., & Rawson, R. A. (2002).

Diaz, R.M., Heckert, A.H., & Sanchez, J. (2005).

Diaz, T., Vlahov, D., Edwards, V., Conover, S., & Moterroso, E. (2002).

Hser, Y., Evans, E., & Huang, Y. (2005).

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**THE ROLE OF TEMPERAMENT IN THE RELATIONSHIP BETWEEN EARLY ONSET OF CIGARETTE SMOKING AND CANNABIS USE. THE TRAILS STUDY.**

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**Aims:** While temperamental characteristics have been related to the onset of cannabis use, it is not clear at what point(s) along the trajectory from early onset of tobacco use (EOT) to early onset of cannabis use (EOC) they exert their impact. This study aims to examine if 1) the relationship between temperament and EOC is mediated by EOT, and 2) temperament moderates the importance of EOT on EOC.

**Methods:** Data from 81% (N=1808) of the participants of TRAILS, a prospective general population study of Dutch adolescents, were analyzed. We used parent-reports on the Early Adolescent Temperament Questionnaire (EATQ-R) to assess the dimensions high-intensity pleasure, frustration, effortful control, shyness and fear at age 10-12. Onsets of tobacco and cannabis use were assessed at, respectively, age 10-12 and 12-15 by means of self-reports. We performed mediation and moderation analyses in Mplus, and controlled for the influences of gender, age and pubertal stage.

**Results:** Findings of the multivariate mediation model showed that high-intensity pleasure and frustration were positively associated with EOC, and that EOT partially mediated these relationships. A higher level of frustration, and for boys a lower level of effortful control, shyness and fear, increased the importance of EOT as a predictor of EOC.

**Conclusions:** Temperamental characteristics play small but significant roles in the entrance to and transition within the substance use trajectory. Gender differences should be considered.

**Support:** Supported by ZonMW research grant 60-60600-98-018.

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**SUBSTANCE-DEPENDENT ANTISOCIAL BOYS: BRAIN PROCESSING OF REWARD/LOSS.**

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**Aims:** Despite losses from risky behaviors, youths with substance and conduct problems (SCP) repeat such behaviors. We hypothesized that their brains process reward and loss differently than others' brains.

**Methods:** 20 adolescent boys being treated for SCP and 20 controls played a computer game during fMRIs. 90 Decision Trials (DTs) required choices between a cautious response (earn \$.01) and a risky response (earn \$.05 or lose \$.10); more losses occurred as the game progressed. 90 Comparison Trials (CTs) presented stimuli similar to DTs, required the same motor response but no decision, and delivered \$.02. After DT responses we examined brain activation for 3.5 sec as win or loss occurred, comparing that to activation during the corresponding CT. We separately considered wins and losses, adjusting activation differences for age and IQ. Contrasts for group differences were: (DT - CT)<sub>Controls</sub> - (DT - CT)<sub>Patients</sub>, and separately (DT - CT)<sub>Patients</sub> - (DT - CT)<sub>Controls</sub>. (Current voxel-wise activation threshold p=0.005, 20 voxel clusters, will be revised for multiple-comparison corrections, p<0.05.)

**Results:** With this game's behavioral schedule the groups did not differ significantly in numbers of risky right presses, wins, or losses. Still, in wins controls' activation significantly exceeded patients' in anterior cingulate cortex, insula, and thalamus; conversely, patients' activation exceeded controls' only in a small area of subcallosal gyrus. In losses controls' activation exceeded patients' nowhere, while patients' activation exceeded controls' in orbitofrontal cortex, dorsolateral prefrontal cortex, subgenual anterior cingulate, and precuneus.

**Conclusions:** After risky behaviors boys with SCP and controls experienced similar numbers of, but activated their brains differently in response to, wins and losses. In risky wins, regions of behavior monitoring and aversion were more activated in controls than in patients. Surprisingly, in losses patients showed more activation in prefrontal areas, and this will be discussed.

**Support:** NIDA grants DA-009842 and DA-011015. The Kane Family Foundation.

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**MORPHINE DECREASES INNATE IMMUNITY RESPONSES IN AN ENDOTOXEMIA MODEL IN TWO STRAINS OF MICE.**

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**Aims:** Morphine modifies innate and adaptive immunological functions through its interaction with mu-opioid receptors. Lipopolysaccharide (LPS), a component of Gram negative bacteria's wall, induces pro-inflammatory cytokine release from macrophages and mast cells through TLR-4 activation. To our knowledge, there are no in vivo studies comparing morphine-induced immunosuppression in different strains of mice. The objective of this work was to evaluate the effects of morphine on the release of two cytokines: the tumor necrosis factor- $\alpha$  (TNF $\alpha$ ) and the monocyte chemoattractant protein-1 (MCP-1 or CCL2), produced by LPS injection in Swiss Webster (SW) and C57BL/6J mice. **Methods:** The optimal time for TNF $\alpha$  and CCL2 secretion after LPS injection (1 mg/kg in 0.3 ml, i.p.) was determined for each strain. Released cytokines were quantified in samples taken from peritoneal washes obtained from animals that received one of the following treatments: a) saline solution; b) morphine (3.1 or 31 mg/kg, i.p.); c) LPS; and d) morphine plus LPS. Additionally, the animals were evaluated in the hot plate test.

**Results:** The results showed that maximal levels of TNF $\alpha$  and CCL2 were achieved 1 h and 2 h after LPS injection, respectively, in both strains of mice. LPS-induced TNF $\alpha$  release was prevented by morphine administration at the two doses tested without significant differences between the strains. On the other hand, morphine was unable to block CCL2 release in SW mice. In C57BL/6J mice, only the highest dose of morphine prevented CCL2 release. Results from the hot plate test showed that morphine produced a dose-dependent antinociceptive effect that was similar in magnitude in both strains of mice.

**Conclusions:** Taken together these results suggest that morphine differentially inhibits cytokine production after LPS injection in SW and C57BL/6J mice.

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**STIGMA FEELINGS ATTACHED TO DRUG DEPENDENCE AND DEPRESSION VARY AS A FUNCTION OF MEDICAL STUDENTS' OWN DEPRESSION HISTORY.**

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**Aims:** Qualitative research suggests that many physicians emerge from their own illness experiences with more empathy and reduced stigma feelings toward patients with stigma-laden conditions. In this quantitative research, we studied variation in stigma feelings of a medical student study population as a function of each student's own personal depression history.

**Methods:** The study population included all medical students on the roster of a required course at their university in Peru (N=120). They were recruited for an anonymous classroom survey, followed by a linked but anonymous online survey with standardized assessment of depression history and stigma (participation level = 73%). Anticipated stigma feelings toward patients were compared, using Christison's standardized multi-item Medical Condition Regard Scale (MCRS) approach for nicotine dependence (ND), alcohol dependence (AD), and depression. Multivariate regression analyses allowed us to estimate stigma feeling levels as a function of each student's depression history (DH).

**Results:** As compared to their classmates, DH-affected students showed more stigma feelings toward ND and AD patients ( $p < 0.05$ ), but stigma feelings toward patients with depression were unaffected by depression history.

**Conclusions:** If empathy and reduced stigma feelings emerge after an episode of depressed mood, the DH effect was not detected in this study. If there is any DH effect, perhaps it causes an increase in stigma feelings with respect to stigmatized conditions such as drug dependence.

**Support:** NIH/FIC/NIDA, D43TW05819, K05DA015799 & T32DA021129

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**FORCED SWIM TEST AND THE ENDOGENOUS CANNABINOID RECEPTOR SYSTEM: EFFECTS OF AN ANANDAMIDE REUPTAKE INHIBITOR AND A FATTY ACID AMIDE HYDROLASE METABOLISM INHIBITOR.**

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**Aims:** In order to explore interactions between stress and the cannabinoid 1 (CB1) system, behavioral responses in the forced swim test (FST) were examined in the presence of an anandamide reuptake inhibitor (AM404) and a fatty acid amide hydrolase (FAAH) metabolism inhibitor (URB597) under acute and sub-chronic conditions. We hypothesize that endogenous cannabinoids (i.e. anandamide) are involved in responses to acute and chronic stress.

**Methods:** C57BL/6J mice (n=7-8) were exposed to the FST (6 min in 32°C water) following vehicle, AM404 (3.2 or 5.6 mg/kg), or URB597 (0.1 or 0.32 mg/kg) treatment under two conditions: acute (one injection 30 min before FST) or subchronic (three injections: one 30 min before FST on Day 1, one 4 hr after FST on Day 1 and one 30 min before FST on Day 2). Immobility was recorded during FST, and corticosterone (CORT) plasma levels drawn from trunk blood were determined with an enzyme immunoassay. Data were analyzed using two-way ANOVA for the time spent immobile and FST day (acute vs sub-chronic). One-way ANOVA was used to analyze CORT levels in response to vehicle vs 5.6 mg/kg of AM404. Significance was set at  $p$  value  $< 0.05$ .

**Results:** The anandamide reuptake inhibitor, AM404, produced a significant increase in immobility at 5.6 mg/kg. Although the effects of URB597 were significant under acute versus subchronic conditions, no dose of URB597 produced a significant increase in immobility. In a subsequent experiment, 5.6 mg/kg of AM404 also increased immobility and CORT under acute FST.

**Conclusions:** Inhibition of anandamide reuptake by 5.6 mg/kg AM404 increased immobility in the FST and this effect correlated with an increase in plasma corticosterone. Parallel increases were not observed with the FAAH inhibitor URB597 at the doses examined in acute FST.

**Support:** Provided by NIH grants R01-DA002749 and T32-007244 and a pre-doctoral fellowship from the UNC-Chapel Hill Graduate School.

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**ACUTE EFFECTS OF BENZYLPIPERAZINE ON COGNITION AND EXECUTIVE FUNCTIONING USING FUNCTIONAL MAGNETIC RESONANCE IMAGING USING THE STROOP PARADIGM-RESULTS FROM THE PILOT STUDY.**

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**Aims:** Party pills containing BZP have been marketed as safe and legal alternatives to illicit recreational drugs, such as 3,4-methylenedioxymethamphetamine (MDMA) or methamphetamine. BZP is a stimulant with similar effects to dexamphetamine (DEX). There is a paucity of information known about the effects of BZP in humans. This study is a randomised double blinded cross-over trial to determine the effects of BZP on impulse control and executive function in comparison to DEX and Placebo using fMRI.

**Methods:** 3 healthy right-handed participants aged 18-40, were recruited from the Auckland area. Subjects were imaged by fMRI, at the Centre for Advanced MRI, at the University of Auckland. Imaging was performed whilst participants undertook the Stroop paradigm 90minutes after an oral dose of BZP(200mg), DEX(20mg) or Placebo. The participants were tested with each condition on a separate occasion. Echo-planar images were collected on a 1.5T scanner (Siemens Magnetom Avanto 1.5 T, Germany).Data was pre-processed, analysed with SPM5 and then used to identify regional activation.

**Results:** BZP and DEX caused changes in activation in the Anterior Cingulate Cortex (ACC) and Dorsolateral Prefrontal Cortex (DLPFC) compared to Placebo, in the congruent, incongruent and overall Stroop (incongruent-congruent) conditions ( $p=0.05$ ). When comparing BZP and DEX there was limited change in the overall Stroop effect ( $p=0.05$ ). Reaction times (RT) and accuracy were compared by the condition and drug state. RT was reduced by BZP and DEX compared to Placebo. There was no trend with accuracy.

**Conclusions:** This pilot study is the first to investigate the effect of BZP on cognition and executive functioning using fMRI. Our results suggest that BZP displays characteristics typical of other psychostimulants such as DEX in the effect on the ACC and DLPFC, and it's effects on RT.

**Support:** Trecia Wouldes

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**THE EFFECTS OF CHRONIC COCAINE ON DELAY-DISCOUNTING IN RATS.**

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**Aims:** This study assesses how impulsive behavior is affected on a delay-discounting task both during and immediately following chronic cocaine administration. Earlier studies have not clearly demonstrated whether preference is altered, or if rats lose the ability to discriminate time or reinforcement magnitude.

**Methods:** Twenty-four male Sprague-Dawley rats were exposed to a delay-discounting task following chronic administration of cocaine (3, 7.5, 15 mg/kg) or deionized water (DI). For all trials, a single lever press to one lever led to one pellet of food immediately, whereas a single lever press to the other lever produced three pellets of food after an adjusted delay (0, 10, 20, 40, 60 s). Rats were exposed to the discounting task for an additional 14 consecutive days following cocaine administration to assess the effects of cocaine withdrawal on impulsivity.

**Results:** Choice for the smaller reinforcer increased as a function of increasing delay ( $p < 0.001$ ), and was exacerbated by chronic cocaine administration ( $p < 0.001$ ). Rats that received 15 mg/kg of cocaine chose the smaller reinforcer significantly more than rats that received DI ( $p < 0.001$ ), and had significantly lower indifference points ( $p = 0.011$ ). Analysis of individual rats' performance indicated that cocaine did not disrupt their ability to discriminate reinforcement magnitude, but caused them to form clear preferences.

**Conclusions:** Chronic cocaine increased the rate at which rats discounted delayed reinforcers. These findings were present both during and following cocaine administration, suggesting that long-term biological changes had taken place. Chronic cocaine decreased rats' choice for the larger reinforcer, indicating a reduction in preference for this reinforcer.

**Support:** Texas Christian University

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**ACTIVELY-USING, NON-TREATMENT-SEEKING MEN WHO HAVE SEX WITH MEN CAN BE SUCCESSFULLY ENROLLED AND RETAINED IN PHARMACOLOGIC STUDIES FOR METHAMPHETAMINE DEPENDENCE.**

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**Aims:** Meth use is prevalent among MSM and is associated with high-risk sexual behavior. We conducted a Phase II study of bupropion vs. placebo to assess the feasibility, safety, tolerability and acceptability of enrolling and retaining actively-using, non-treatment-seeking meth-dependent MSM into a pharmacologic intervention.

**Methods:** Meth-dependent, sexually-active MSM were randomized to receive daily bupropion (N=20) or placebo (N=10) for twelve weeks. Eligibility criteria included meth-positive urine, high-risk sexual behavior, and meth dependence by SCID. Participants received weekly substance use and sexual risk-reduction counseling, provided weekly urine specimens and completed monthly ACASI self-report of drug use. Adherence to study drug was measured by MEMS caps and defined as the number of distinct MEMS cap openings divided by the number of expected daily doses.

**Results:** Participants were meth-dependent MSM (53% White, 20% Hispanic, 10% Black, 16% Other), of whom 43% were HIV-positive. Ninety percent (27/30) completed the trial: 89% of the monthly ACASI risk assessments were completed (Bupropion 87%, Placebo 93%;  $p=0.21$ ), 81% of all study visits were attended (B 80%, P 81%  $p=0.22$ ), and 81% of all scheduled weekly urine samples were collected (B 80%, P 81%  $p=0.22$ ). No serious adverse events occurred. There were no significant differences in adverse events by treatment assignment ( $p=0.11$ ). Adherence to medication was 60% (B 59%, P 62%;  $p>0.8$ ) and 95% reported satisfaction with study participation.

**Conclusions:** Bupropion was safe and well-tolerated. It was feasible to enroll and retain a significant majority of actively-using, non-treatment-seeking meth-dependent MSM in a pharmacologic intervention. While study participation rates were high, study drug medication adherence was moderate. Further studies should include a larger trial with improved adherence support to evaluate the efficacy of bupropion treatment for meth dependence.

**Support:** K23 DA016231;R21 DA021090;P50 DA18185

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**ACUROX® (OXYCODONE HCL/NIACIN) TABLETS FOR THE TREATMENT OF ACUTE, MODERATE TO SEVERE PAIN FOLLOWING BUNIONECTOMY SURGERY IN ADULT PATIENTS.**

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**Aims:** Prescription opioid analgesics, particularly short-acting opioids, are mis-used and abused by excessive ingestion of intact tablets, and by intra-nasal and intravenous administration. Thus, there is a need for short-acting opioids designed to discourage inappropriate use. ACUROX® Tablets (ACUROX) are a unique combination of short-acting oxycodone HCl for moderate to severe pain, and niacin. At doses exceeding the recommended 2-tablet dose, ACUROX is associated with transient niacin-induced unpleasant, dysphoric effects. Additional functional excipients challenge common physical and chemical manipulations. Analgesic efficacy and safety of ACUROX were evaluated in a Phase III study of adults with acute, moderate to severe pain following bunionectomy surgery.

**Methods:** After meeting eligibility criteria, 405 patients were randomized in a 1:1:1 ratio to receive 2 ACUROX (oxycodone HCl/niacin) 7.5/30mg, 2 ACUROX 5/30mg, or placebo every 6 hrs for 48 hrs after surgery.

**Results:** Both ACUROX doses demonstrated significantly superior reductions in pain intensity compared with placebo as evidenced by the primary endpoint, the time-weighted sum of pain intensity differences over 48 hrs (SPID48;  $P<0.0001$  and  $P=0.0001$  for ACUROX 2 x 7.5/30mg and ACUROX 2 x 5/30mg, respectively). Analysis of secondary efficacy measures, including responder analysis and time-weighted total pain relief (TOTPAR<sub>0</sub>) over 6 hrs following first administration, confirmed that each dose level was significantly superior to placebo. Six patients discontinued treatment with ACUROX due to treatment-emergent adverse events (AEs): 2 patients (1.5%) in the ACUROX 5/30 group and 4 patients (3.0%) in the ACUROX 7.5/30 group. AEs were consistent with known effects of oxycodone HCl and niacin; most were mild or moderate in severity, and no serious AEs occurred.

**Conclusions:** This is the first large clinical study demonstrating the efficacy and safety of a short-acting opioid composition designed to deter excessive oral ingestion.

**Support:** King Pharmaceuticals®, Inc.

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**DO PARTICIPANTS IN RANDOMIZED CLINICAL TRIALS FOR NICOTINE DEPENDENCE REFLECT THE GENERAL POPULATION OF SMOKERS?**

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**Aims:** To test the extent to which eligibility criteria for randomized clinical trials (RCTs) for medications to assist smoking cessation and/or relapse prevention predict generalizability.

**Methods:** Individuals with nicotine dependence (n=4962) were identified from National Epidemiologic Survey on Alcohol and Related Conditions. We applied common eligibility criteria from RCTs & estimated the proportion of the original sample remaining. Population-level differences were analyzed between enrollees, general population eligibles and community-dwellers.

**Results:** Sequential application of eligibility criteria would allow 25.7% of community-dwelling nicotine dependent individuals to participate in RCTs. The inclusion criterion with greatest impact was smoking shortly after waking (eliminated 16%). Greatest reduction were due to exclusion criteria for Axis I disorders (30%), substance use disorders (25%), and use of non-cigarette tobacco (15%). Those eligible were more likely to be employed (X2 92.4, 8df,  $p<0.01$ ) and have health insurance (X2 38.3, 3df,  $p<0.01$ ) than non-eligible community-dwelling individuals. Compared to the RCTs, application of criteria differentially excluded younger individuals (early- to mid-20s), and enriched for those smoking more cigarettes per day & for longer, compared to community-based individuals.

**Conclusions:** Nearly 3/4 of those with nicotine dependence in the general population would not be eligible for participation in RCTs. These findings suggest clinical trials samples might not be representative of community-dwelling populations, limiting the generalizability of RCT outcomes. Smokers in their 20s may also not respond to nicotine replacement therapy in the same manner as those enrolling in RCTs. This could mean that therapeutic effects observed in RCTs might not be the same in the general population. Therefore enrollment criteria may benefit from modification to better represent expected effectiveness in the general nicotine dependent population.

**Support:** This research was supported by GlaxoSmithKline.

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**MORPHINE ANTINOCICEPTION IN COMBINATION WITH METABOTROPIC GLUTAMATE RECEPTOR (MGLUR) ANTAGONISTS.**

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**Aims:** The present study examined the effects of morphine alone and in combination with the group 5 metabotropic glutamate receptor (mGluR5) antagonist, 2-methyl-6-(phenyl-ethynyl) pyridine hydrochloride (MPEP) and the group 1 metabotropic glutamate receptor (mGluR1) antagonist (3,4-dihydro-2H-pyran-2,3-b[quinolin-7-yl)-(cis-4-methoxycyclohexyl)-methanone (JNJ) in the hot plate and tail withdrawal procedures in rats.

**Methods:** Baseline latencies to withdraw the distal portion of the tail from a 52°C hot water bath and lick the hind paw following exposure to a 52°C hot plate were determined in male Fischer 344 rats. Following baseline determinations, morphine (0.3-30.0 mg/kg) was administered i.p. according to a cumulative dosing schedule, with the first dose given either alone or in combination with the mGluR5 antagonist MPEP (3.0-10.0 mg/kg, i.p.) or the mGluR1 antagonist JNJ (1.0-3.0 mg/kg, i.p.). After 15 minutes, latencies in both the tail withdrawal and hot plate were determined following each cumulative dose of morphine.

**Results:** Neither MPEP nor JNJ increased morphine's antinociceptive effects in the tail withdrawal procedure. Although MPEP did not increase morphine's effects in the hot plate procedure, JNJ (1.0mg/kg) produced a significant 5-fold, leftward shift in the morphine dose effect curve, decreasing the morphine ED<sub>50</sub> from 23.8 mg/kg following morphine alone to 5.0 mg/kg in combination with JNJ.

**Conclusions:** These results indicate that increases in morphine antinociception following pretreatment with the mGluR1 antagonist JNJ and the mGluR5 antagonist MPEP depend on the particular antagonist and the type of assay used to examine antinociception.

**Support:** Ro1-DA002749 and T32-DA007244.

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**OPIOID RECEPTOR MEDIATION OF MORPHINE'S DISCRIMINATIVE STIMULUS EFFECTS IN THE INBRED FISCHER 344 AND LEWIS RAT STRAINS.**

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**Aims:** The F344 and LEW inbred rat strains differ on a number of morphine-induced behaviors. The present experiment assessed their ability to acquire a morphine discrimination (using the taste aversion baseline of drug discrimination learning) and the relative roles of the mu, kappa and delta opioid receptor subtypes in this discrimination.

**Methods:** Specifically, F344, LEW and outbred Sprague Dawley (SD) male rats received an injection of morphine (5.6 mg/kg; i.p.) 30-min prior to 20-min saccharin access which was followed by an injection of lithium chloride (1.8 mEq; F344: n = 8; LEW: n = 8; SD: n = 4) or distilled water (F344: n = 8; LEW: n = 7; SD: n = 4); three recovery days followed during which saline preceded saccharin access. Specific agonists for the kappa [(-)-U50,488H, 0.16-5 mg/kg], delta [SNC80 (0.32-18 mg/kg)] and mu [heroin (0.10-1.8 mg/kg)] opioid receptors, respectively, were then tested for their ability to generalize to the morphine cue.

**Results:** All three strains displayed comparable acquisition of the morphine discrimination and displayed similar morphine dose-substitution curves (1.0-10.0 mg/kg). Paired-samples t-tests revealed that 1.0 and 1.8 mg/kg heroin generalized fully to the morphine training dose in F344 and SD rats. The F344 rats also displayed partial generalization of the 0.56 mg/kg dose of heroin. The LEW strain displayed only partial generalization at 1.8 mg/kg heroin. No strain displayed generalization to any dose of (-)-U50,488H or SNC80 tested.

**Conclusions:** The fact that neither kappa nor delta compounds substituted for morphine suggests that morphine stimulus control in these strains is solely mu mediated. The basis for the differential substitution by heroin (despite comparable morphine control) suggests differential mediation of the morphine and heroin cues.

**Support:** Supported by a grant from the Mellon Foundation to ALR and intramural funds from NIDA and NIAAA.

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**HPA AXIS RESPONSE TO PSYCHOLOGICAL STRESS IS PREDICTIVE OF TREATMENT RETENTION IN RESIDENTIAL SUBSTANCE ABUSE TREATMENT.**

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**Aims:** High rates of treatment dropout occur in substance abuse treatment programs, leading to an increased risk for relapse to drug use. Negative reinforcement models of addiction emphasize an individuals' inability to tolerate stress as a key factor for understanding poor substance use treatment outcomes, and evidence indicates that dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis contributes to an individual's inability to respond adaptively to stress. The aim of the current study was to examine whether HPA axis response to stress is predictive of treatment retention among a sample of drug users in residential substance abuse treatment.

**Methods:** Prospective study assessing treatment retention among 102 individuals enrolled in residential substance abuse treatment. Participants completed two computerized stress tasks, and HPA axis response to stress was measured via salivary cortisol at five time points from baseline to 30 minutes post stress exposure.

**Results:** The main outcome measures were treatment dropout (categorical) and total number of days in treatment (continuous). Significantly elevated salivary cortisol response to stress was observed in participants who dropped out compared to treatment completers. Cox proportional hazards survival analyses indicated that a higher peak cortisol response to stress was associated with a shorter number of days to treatment dropout.

**Conclusions:** Results indicate that elevated HPA axis response to stress is associated with an inability to remain in substance abuse treatment. These findings provide preliminary support for biological markers of stress induced treatment failure, and the development and implementation of treatments targeting this vulnerability.

**Support:** NIDA R21DA022741 (PI: Daughters)

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**LOCKED UP FROM PAIN OR PILLS: THE CRIMINALIZATION OF PAIN AND POVERTY.**

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**Aims:** The relationship between diverters/sellers of pain medication with their health care providers focusing upon pain patients who resell large quantities of prescription opioids (POs) in the street markets. The aim address two related issues: 1) difficulties and dangers faced by the population of PO diverters/sellers who need pain relief, and 2) response(s) of doctors/public health and law enforcement to increasing use and misuse of POs.

**Methods:** PO users among street drug users largely consists of aging and/or injured poor persons. Staff have located and conducted voice-recorded qualitative interviews with 52 diverters of POs, following a checklist of topics. All subjects report reselling POs and obtaining a substantial portion of their income from such PO sales. Interview transcripts analyze the relationship between the medical and law enforcement system as understood by these PO diverter/seller pain patients.

**Results:** During 2008, NYC police seek to reduce the diversion of POs ; many doctors now require urine specimens to confirm PO consumption. Diverter/sellers report more difficulty obtaining POs. Pain patients experience the simultaneous and mixed emotions of being helped with their pain, yet suspected of crimes. The street-drug-using PO patient also sends mixed messages, having a sincere intent to remedy their own pain, yet have pressing financial needs. The levels of fear and distrust between drug-using patients and medical professionals may harm pain treatments. The mixed messages are also driven by very real financial motives on both sides of the relationship.

**Conclusions:** The relationship between medical practitioners and street drug using pain patients has been criminalized to an extent that it may be harmful for treatment. Most of the diverters/sellers experience financial pressures often as compelling as the pressure to relieve their real pain, as many balance between selling enough medication to pay their bills and taking enough to function. To reduce the criminalization of the relationship between street-drug-using pain patients and their health care providers the profit motives driving the behavior of both parties needs to be decreased.

**Support:** NIDA R01 DA021379-01

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**ALCOHOL AND SUBSTANCE USE IN TRAFFIC ACCIDENT VICTIMS OF PORTO ALEGRE, BRAZIL.**

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**Aims:** To estimate the prevalence of alcohol/substance use and test its association with risk behaviors and drug abuse/dependence in traffic accident (TA) victims who were admitted in two major trauma centers of a state capital.

**Methods:** Cross-sectional study with convenience sample selected among October 10 and November 18, 2008. Inclusion: drivers, passengers or pedestrians above 18 were admitted for TA. Data: structured interview was collected with PDAs connected to a virtual database, 24/7, and alcohol level was estimated by breathalyzer. Saliva or urine tests were used to screen for THC, cocaine, amphetamines and benzodiazepines. Analysis: chi-square and ANOVA tests were used for bivariate comparisons; logistic regression was run for adjusting confounders. Significance level was .05.

**Results:** 92.6 % of the eligible sample was approached; 10.9% refused to participate. The sample was composed by 604 subjects with mean age of 32.8 +/- 13.2, 72% male; most (60%) were drivers(80% motorcycle), and 42% had previous TA. Positive BAC was found in 8.7% of sample, but 28.5% of the subjects referred alcohol use in the 24h hours prior to the TA. 10% of drug tests were positive. Drivers were more significantly men, younger, more educated and more prone to binge drinking. The only factor associated with positive BAC was binge drinking in the last year(OR 3.9 IC 95(2.3 – 6.7)).

**Conclusions:** In Brazil there are 36,000 TA deaths every year, but few studies on its association with alcohol and drug use. Data suggest that drivers, passengers and pedestrians are exposed to different risk factors which could imply in specific public policies for each group. The number of motorcycle drivers was alarming, since only 11% of vehicles in this city are motorcycles. This is a relevant finding that can represent an emerging public health problem and needs further investigation.

**Support:** SENAD (Secretaria nacional de políticas sobre drogas)

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**COCAINE REWARDS SEGREGATE NEURAL PROCESSING UNDERLYING PERFORMANCE OF COGNITIVE TASKS IN NONHUMAN PRIMATES.**

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**Aims:** Analyses of behavioral, neurophysiologic and imaging data in nonhuman primates (NHPs) performing two different well-trained cognitive tasks, show that trials that signal delivery of cocaine and juice rewards activate different subpopulations of dorsal and ventral striatal neurons, which is reflected in differential activation of dorsal and ventral striatum in brain images of local cerebral metabolic activity from the same animals.

**Methods:** Methods: Rhesus monkeys were trained to perform a 1) multi-image delayed-match-to-sample (DMS) or 2) GoNogo, task in order to receive either cocaine (IV) or juice as a reward for successful performance on individual trials. PET imaged [18]FDG was employed to visualize local cerebral glucose metabolic rates while animals performed the tasks. Recordings were also obtained from neurons in the dorsal and ventral striatum.

**Results:** Accuracy on cocaine trials was dose-dependent and produced different types of brain activation patterns using PET [18]FDG imaging than sessions employing only juice rewarded trials. Neurons in dorsal and ventral striatum recorded during task performance reflected a complex hierarchical segregation within trial events that was associated with either isolated responses on only cocaine or juice trials, or firing on both types of trial in completely different sets of cells.

**Conclusions:** The findings suggest that cocaine rewards activate different neural systems within the brain than juice rewards and that cocaine is capable of "hijacking" normal reward processes that are activated by appetitive conditioning. However, a larger percentage of neurons in dorsal and ventral striatum responded indiscriminately to both types of rewards, suggesting that some reward systems cannot discriminate between cocaine and appetitive elements delivered in a behaviorally contingent manner. This bias in number of striatal neurons that respond to both types of rewards makes these brain regions more susceptible to activation when substances are abused.

**Support:** This work was supported by DA06634 and DA0235373 and N00014-06-1-0397 to S.A.D

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**SUBSTANCE USE AND AGGRESSION IN THE ADOLESCENT OFFSPRING OF TEENAGE MOTHERS.**

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**Aims:** Teenage mothers and their offspring appear to be at greater risk of substance use even after controlling for the effects of lower SES. Recent studies provide evidence for a strong genetic component for both adolescent substance use and problem behavior. The goal of the current study is to examine the association between adolescent substance use and aggression in the 14-year-old offspring of teenage mothers.

**Methods:** Mothers were recruited as pregnant teenagers (n = 416; age range = 12-18 yrs 68% African-American) from an outpatient prenatal clinic. Data collection at the 14-year phase is ongoing (n = 241 tested to date). Mothers reported on their SES and current substance use. Offspring reported on their own substance use (29% were ever smokers, 18% ever drinkers, and 20% marijuana users). Current maternal hostility (Spielberger, Gorsuch, & Lushene, 1970) and adolescent aggression (CBCL: Achenbach, 1991) were also measured.

**Results:** The White offspring of teenage mothers were significantly more likely to have used alcohol (43%) than Black offspring (23%). Current maternal marijuana use and girls' smoking by age 14 were associated with increased aggression in the daughters of teenage mothers (Adj R<sup>2</sup> = .15, F = 5.05, p < .01). In contrast, maternal hostility, adolescent smoking and marijuana use by age 14 were associated with increased aggression in the sons of teenage mothers (Adj R<sup>2</sup> = .28, F = 5.40, p < .001).

**Conclusions:** Conducting separate multivariate analyses on male and female offspring of teenage mothers allowed us to identify different correlates of aggressive behavior problems in the sons and daughters from these vulnerable families. Maternal substance use (specifically, current marijuana use) was associated with girls' aggression and maternal levels of hostility were associated with boys' aggression. Adolescent offspring of teenage mothers who smoked had significantly higher aggression scores than non-smoking offspring of both sexes, consistent with problem behavior theory and research linking hostility and aggression to health-risk behavior.

**Support:** NIDA 09275 (PI: MC), NIAAA T32 07453 (PI: MC), and the University of Pittsburgh.

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**PREDICTING ADHERENCE TO TREATMENT FOR METHAMPHETAMINE DEPENDENCE FROM NEUROPSYCHOLOGICAL AND DRUG USE VARIABLES.**

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**Aims:** No prior studies have examined whether neurocognitive functioning is associated with outcome of treatment for methamphetamine (MA) dependence. We sought to predict treatment outcome from baseline neurocognitive performance in an outpatient clinical trial for MA dependence. We also compared the predictive value of cognitive performance to several other drug use and psychiatric variables to determine relative strength of predictive power.

**Methods:** In an outpatient clinical trial of bupropion combined with cognitive behavioral therapy and contingency management (Shoptaw et al., 2008), 60 MA-dependent adults completed three tests of reaction time and working memory at baseline. Other variables collected at baseline included measures of drug use, mood/psychiatric functioning, employment, social context, legal status, and medical status. We evaluated the relative predictive value of all baseline measures for treatment outcome using Classification and Regression Trees (CART; Breiman, 1984), a nonparametric statistical technique that produces easily interpretable decision rules for classifying subjects that is particularly useful in clinical settings. Outcome measures were whether or not a participant completed the trial and whether or not most urine tests showed abstinence from MA abuse.

**Results:** Urine-verified MA abuse at the beginning of the study was the strongest predictor of treatment outcome; other psychosocial measures (e.g., nicotine dependence and Global Assessment of Functioning) offered some predictive value. Cognitive variables did not significantly aid prediction alone or in conjunction with MA abuse at the beginning of the study.

**Conclusions:** On the basis of these findings, we recommend that research groups seeking to identify new predictors of treatment outcome compare the predictors to MA usage variables to assure that unique predictive power is attained.

**Support:** DA022539, DA18185

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**PATTERN OF ALCOHOL USE AND ASSOCIATED FACTORS: A CROSS-SECTIONAL STUDY IN A FRENCH EMERGENCY ROOM.**

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**Aims:** Little is known about prevalence of alcohol use among patients attending emergency room (ER) services in France. The aim of this study was to describe the patterns of alcohol use and associated factors among a sample of patients attending ER of a University Hospital (CH Saint André, Bordeaux) from March 10th to 24th 2005.

**Methods:** All consecutively admitted patients to the ER were assessed with a questionnaire. Data gathered concerned sociodemographic data, lifetime and current frequency and amount of alcohol, tobacco, and cannabis use. The CAGE-cannabis and the FACE were used to assess modalities of use of cannabis and alcohol.

**Results:** 509 patients were screened. 60% were current alcohol users. They were mostly men, tobacco smokers, and had experimented cannabis at least once lifetime (respectively 65%, 54% and 35% of alcohol users).

40% were "problematic users" and 30% were likely to be alcohol-dependent. Factors associated to a "problematic use" of alcohol were an admission caused by consequences of alcohol use (OR=17,6), being current cannabis user (OR=44,9), being less than 30 (OR=1,8), and previous psychiatric care (OR=3,1). Same factors were even more associated to a risk of alcohol dependence (31-55 y.o. being the most represented age group).

**Conclusions:** ER are specific environments where more heavy drinkers could be found compared to general population. As they presented also several comorbid behaviors it seems interesting to make a systematic screening of alcohol in ER for early identification and management of problem drinking.

**Support:** UB2, INSERM IFR99, CHU

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**DRAMATIC ELEVATIONS IN EXTRACELLULAR GLUTAMATE WITHIN THE MEDIAL PREFRONTAL CORTEX OF RATS DURING EXTENDED ACCESS TO COCAINE SELF-ADMINISTRATION.**

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**Aims:** We have previously reported that extended (6 hrs/day), but not brief (1 hr/day), access to self-administered IV cocaine results in increased expression of the NR2 subunits of NMDA receptors within the mPFC 14 days to 2 months after withdrawal. In addition, blockade of NMDA receptors within the mPFC blocked the escalation of cocaine self-administration in extended access subjects, while leaving self-administration in saline controls or brief access subjects unaltered. Our results are consistent with the hypothesis that extended access to cocaine self-administration results in increased release of glutamate within the mPFC, and that this increased release of glutamate within the mPFC is important for the development of escalated cocaine consumption. The present study was designed to test this hypothesis

**Methods:** Rats were trained to lever press for 0.25 mg/infusion cocaine during 7 daily 1-hr sessions, and then allowed either 1 last daily session of 1 hr, or 10 more daily sessions of 6 hrs, access to cocaine self-administration. Glutamate levels within the mPFC were monitored during the first and eighth session in brief access animals, and during the eighth and seventeen sessions (i.e. first and last 6-hrs sessions) in extended access animals

**Results:** Brief access to cocaine self-administration resulted in decreased glutamate levels within the mPFC of both drug-naïve and drug-experienced animals. In contrast, extended access to cocaine self-administration resulted in increased glutamate levels within the mPFC that was exacerbated on the tenth session of cocaine self-administration

**Conclusions:** These data support our hypothesis that extended access to cocaine self-administration results in increased glutamate release within the mPFC, which plays a critical role in the development of escalated cocaine self-administration, a critical symptom of addiction

**Support:** Supported by NIDA grants: DA017104 to OBS and DA024038 to KKS

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**EMPLOYMENT-BASED ABSTINENCE REINFORCEMENT AS A MAINTENANCE INTERVENTION FOR THE TREATMENT OF PERSISTENT COCAINE USE IN METHADONE PATIENTS WITH 24-MONTH FOLLOW-UP.**

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**Aims:** Determine whether employment-based abstinence reinforcement is an effective treatment for cocaine addiction during a long-term maintenance intervention and at 18- and 24-month follow ups.

**Methods:** Unemployed cocaine dependent welfare recipients who used cocaine while enrolled in methadone treatment in Baltimore (N=128) were enrolled in a 6-month job training and abstinence initiation program. Participants who initiated abstinence, attended regularly, and developed required job skills were hired as operators in a data entry business and randomly assigned to an employment only (EO, n = 24) or abstinence-contingent employment (AE, n = 27) group. AE participants received one year of employment-based abstinence reinforcement, in which access to paid employment was contingent on provision drug-free urine samples under routine and then random drug testing. If an AE participant provided drug-positive urine or failed to provide a mandatory sample, then that participant received a temporary reduction in pay and could not work until urinalysis confirmed recent abstinence.

**Results:** During the year of employment, AE participants provided more cocaine-negative urine samples than EO participants (79% and 51%, respectively; p = 0.004, OR = 3.73, 95% CI = 1.60 – 8.69). At 18- and 24-month follow-ups, AE and EO groups provided similar percentages of cocaine-negative urine samples (18-month, 54% for both groups; 24-month, 50% and 57%, respectively, p = 0.89).

**Conclusions:** Employment-based abstinence reinforcement with random drug testing is an effective long-term maintenance intervention for cocaine addiction, but its effects are not maintained after the contingencies are discontinued. Workplaces could serve as therapeutic agents in the treatment of drug addiction by arranging long-term employment-based abstinence reinforcement contingencies. Arrangements that include indefinite employment are preferable to arrangements that include fixed periods of employment.

**Support:** National Institute on Drug Abuse grants R01DA13107 and T32DA07209

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**VALIDITY OF THE GAMBLING SECTION FOR THE FRENCH ADAPTATION OF THE ADDICTION SEVERITY INDEX.**

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**Aims:** Similarities exist between pathological gambling and substance use disorders. As gambling disorders and substance use disorders have shared problems, similar instrument should be useful for assessing severity of problems. The most widely used instrument to assess the severity of substance use is the Addiction Severity Index (ASI). Objective: to assess the psychometric properties of the Gambling section for the French adaptation of the ASI.

**Methods:** Participants were recruited among patients who enrolled in an addiction treatment program. They were assessed with the adaptation of the ASI and the South Oaks Gambling Screen (SOGS).

**Results:** All solicited subjects (n=52) agreed to participate. All were assessed as pathological gamblers and were in treatment for gambling problems. They were in average 44.6 y.o. (SD=10.7), 47 were male. They gambled 14.8 days (SD=12.3) in average over the last 30 days for 8.9 years (SD=12.1) in average. They also used alcohol (n=38), tobacco (n=41), benzodiazepines (n=18), and more rarely other substances (cannabis, opiates, cocaine). The participants presented severity scores less than 4 for all domains assessed by the ASI except for the gambling section. The mean score of the SOGS was 12.5 (SD=2.7). Considering the score of the SOGS as the reference, sensibility and positive predictive value of the ASI gambling score were 85.7%. The specificity and negative predictive value were 50%.

**Conclusions:** These results suggested that the adaptation of the ASI for gambling assessment may be a valid tool for assessing severity of gambling problems. It provides more data than a screening tool and could be useful to characterize more precisely the gamblers.

**Support:** Université de Bordeaux and Université de Nantes



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**THE RELATIONSHIP BETWEEN INCREASED EXERCISE AND REDUCED SUBSTANCE USE.**

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**Aims:** Exercise is increasingly recognized as an important aid in helping people to manage multiple chronic conditions in general and sustaining recovery from substance use disorders specifically. The goal of this observational study is to evaluate the extent to which increased physical exercise is associated with reduced concurrent substance use in the same quarter and the extent to which any gains are sustained into the next quarter.

**Methods:** Data are from 446 participants in the Early Re-Intervention (ERI) experiments (Dennis & Scott, 2007; Scott & Dennis, under review) who were interviewed using the Global Appraisal of Individual Needs (GAIN) quarterly for 3 years (over 95% completion per wave, 82% completing all waves). Participants were 54% Male, 80% African American, 77% between the age of 30-49, 88% with dependence, 56% with co-occurring psychiatric problems, and 54% with moderate to high levels of crime and violence. They were recruited (93% participation) from sequential substance abuse treatment admissions at Haymarket Center's central intake on the west side of Chicago. Each quarter participants were classified into those who increased their days of exercising 20 or more minutes per day versus those who did not (including those who decreased their exercise).

**Results:** Increased exercise was associated with significantly greater reductions in substance use in the same quarter (Cohen's  $d = -0.43$ ,  $t(845) = 6.14$ ,  $p < .0001$ ), and the resulting differences were sustained in the next quarter (Cohen's  $d = 0.00$ ,  $t(412) = -0.09$ ,  $p = .9999$ ).

**Conclusions:** Increasing exercise was associated with moderate reductions in substance use over the same time and that these gains appeared to be subsequently sustained. This suggests that increasing exercise may be a useful tool in supporting recovery and should be explored further in a prospective experiment.

**Support:** National Institute on Drug Abuse Grant # R37 DA11323.

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**PROGESTERONE ATTENUATES CHRONIC COCAINE-INDUCED REARING RESPONSES BUT NOT DENDRITIC SPINE INCREASES IN THE NUCLEUS ACCUMBENS CORE OF FEMALE RATS.**

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**Aims:** In clinical and pre-clinical studies, progesterone has been shown to attenuate cocaine-induced reward and locomotor responses in female rats. This study aimed to determine if progesterone administration reduces cocaine-induced psychomotor activity and/or morphological changes in the core of the nucleus accumbens (NAc).

**Methods:** To this end, Fischer rats (8 weeks,  $N = 100$ ) were divided into two experimental conditions. For acute progesterone treatments, rats received 13 days of saline and hormone vehicle and on day 14 a single dose of progesterone (500ug; s.c.) or vehicle (sesame oil) four hours before saline or cocaine (15 mg/kg; i.p.) administration. For chronic progesterone treatment, rats received 14 days of progesterone (500 ug; s.c. four hours before drug treatment) and saline or cocaine (15 mg/kg; i.p.). Psychomotor responses were recorded using an automated computerized apparatus for 1 hour post drug treatment.

**Results:** Overall, cocaine increased psychomotor activation. Chronic progesterone administration reduced rearing counts after chronic cocaine treatment [ $F(1, 70) = 4.346$ ,  $p = 0.021$ ]. Animals in the chronic cocaine and progesterone group also showed significant increases in dendritic spines in the NAc compared to animals in the acute-treatment group [ $F(1, 19) = 3.1109$ ,  $p = 0.005$ ].

**Conclusions:** These results suggest that although progesterone may play a regulatory role in mediating cocaine-induced behaviors in female rats, it may do so without affecting cocaine-induced anatomical adaptations in the NAc.

**Support:** Supported by: SCORE 506-GM60654, MBRS-RISE GM60665, and DA00325.

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**CONGRUENCE OF SELF-REPORTED DRUG USE WITH URINE TOXICOLOGY SCREENING IN A SUBSTANCE ABUSE TREATMENT POPULATION.**

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**Aims:** The validity of self-reported drug use data is always a concern in clinical studies. In a recent study to validate a number of screening tools for mental disorders in a substance abuse treatment population, self-report data on drug use and urine samples for toxicology screening were collected. The purpose of this study was to examine the congruence of self-reported recent drug use with urine drug screening results.

**Methods:** 543 clients were recruited from three large treatment centres in Ontario, Canada (68.7% male; mean age 37.3 years). Clients completed several screening tools and self-report measures, followed by independent same-day structured clinical interview (SCID), and a urine sample was collected for toxicology screening (immunoassay and broad spectrum drug screening using automated HPLC). Self-reported drug use (captured by the Psychoactive Drug History Questionnaire) was then compared to the urinalysis results. A coding system was developed to capture the degree of congruence between the self-report data and laboratory data, taking recency of reported use and urine drug concentrations into account.

**Results:** A total of 322 (59.3%) clients had a positive urine screen for at least one substance. 228 males (61.1% of all male clients) and 94 females (55.3% of all female clients) had a positive urine screen for at least one substance. The most common substances that appeared in the urine screens were cannabinoids (38.3%), cocaine (24.5%), and prescription/OTC opioids (12.2%). 92.8% of those testing positive for cannabinoids, 80.5% of those testing positive for cocaine, and 77.3% of those testing positive for prescription/OTC opioids self-reported use that matched the urine screen results.

**Conclusions:** In general, there was high congruence between the self-reported data and the results of the urine drug screens. Given that urinalysis may not always be feasible or practical in some situations, these findings lend greater confidence in the accuracy of self-reported drug use data.

**Support:** Canadian Institutes for Health Research.

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**AN ANALYSIS OF SUBSTANCE ABUSE TREATMENT OUTCOMES BETWEEN A SAMPLE OF AMERICAN INDIANS/ALASKA NATIVES AND A COMPARISON GROUP.**

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**Aims:** The primary aims of this study are to compare the following characteristics between a sample of American Indians/Alaska Natives and a matched comparison group receiving substance abuse treatment: 1) pretreatment medical, psychiatric, and psychosocial characteristics, 2) services received during substance abuse treatment, and 3) treatment outcomes.

**Methods:** Data retrieved from the Treatment Impact System (TSI) project and Methamphetamine Treatment Project (MTP) were used to compare substance abuse treatment measures between a sample of American Indians/Alaska Natives ( $n=279$ ) and a matched comparison group ( $n=279$ ). Main outcome measures included the Addiction Severity Index (ASI), Treatment Services Review (TSR), and self-rating scales of physical health and functioning. With regard to treatment outcomes,  $t$  tests were utilized to assess whether changes in ASI composite scores from admission to follow-up were significantly different from zero and ANCOVA was utilized to examine the differences between American Indians/Alaska Natives and controls on ASI composite scores.

**Results:** No significant substance abuse treatment outcome differences were observed between the American Indian/Alaska Native sample and the matched comparison sample at 12-months post-treatment based on legal, employment, medical, and psychiatric measures. However, American Indians/Alaska Natives received significantly more family and abuse-related services and completed treatment less often. Also, American Indians/Alaska Natives demonstrated significantly more medical and psychiatric problems at baseline.

**Conclusions:** More comprehensive services for American Indians/Alaska Natives may be required in order to achieve similar substance abuse treatment outcomes observed in the general U.S. population. Addressing health-related disparities in this population may aid providers towards providing adequate and culturally-relevant treatment for American Indians/Alaska Natives with substance abuse problems.

**Support:** This study was supported in part by the National Institute of Drug Abuse grants P30 DA016383, and K05DA017648.

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**POST SURGERY PATIENT-CONTROLLED ANALGESIA IN SMOKERS AND NON-SMOKERS.**

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**Aims:** Patient controlled analgesia (PCA) use in women after post cesarean surgery was higher in smokers compared to non-smokers. In joint-replacement patients PCA use was inversely related to pre-surgery sleep. This study assessed sleep and PCA morphine use in smokers vs. non-smokers undergoing joint replacement surgery.

**Methods:** Volunteers were 33 joint-replacement patients (11 smokers, 2M, 9F; 22 non-smokers 8M, 14F) from ages 40-84 yr. They completed a questionnaire that included questions about sleep, nicotine use, other drug use, and co-morbid disorders. Smokers reported using 3-30 cigarettes/day. Nicotine use was discontinued upon entering the hospital the day of surgery. After surgery and anesthesia recovery, each received pain medication with a PCA device that limited doses of intravenous morphine to 1mg every 10 min. PCA number of injections and denials (requests during 10-min lockouts) were recorded hourly for 24 hr post-surgery.

**Results:** The 24-hr average number of denials ( $p < .002$ ) and injections ( $p < .008$ ) were greater in smokers than non-smokers (62 vs. 14 and 46 vs. 27). By hour, smokers had more denials ( $p < .007$ ) and more injections ( $p < .014$ ) in each of the first 6 hr, while not differing in the last 18 hr. Plots of denials and injections as a function of time-of-day revealed a spike in denials ( $p < .001$ ) in smokers vs. non-smokers that coincided with self-reported time of arising. Pre-surgery sleep and drug use reports did not differ between groups.

**Conclusions:** These data show a history of smoking and acute abstinence over the 24-hr surgery and recovery period is associated with increased analgesia seeking (morphine denials and injections) behavior. Hourly patterns suggest that pharmacologic (duration of nicotine abstinence) and behavioral factors (smoking at time of awakening) mediate analgesic seeking in smokers.

**Support:** The Fund for Henry Ford Hospital, B10914 awarded to Dr. Roehrs.

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**COGNITIVE DISTINCTIONS BETWEEN CURRENTLY USING AND ABSTAINING METHAMPHETAMINE-DEPENDENT INDIVIDUALS.**

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**Aims:** Recent research indicates that methamphetamine users exhibit impairments in cognition compared to non-drug users. Of practical concern is whether abstinence reduces these deficits in methamphetamine users. With data collected in the 3-year follow-up of the Methamphetamine Treatment Project, we assessed the influence of abstinence on two cognitive domains in which methamphetamine users have been found to exhibit deficits.

**Methods:** A total of 409 methamphetamine dependent individuals completed interviews regarding their drug use and completed tests of attention and memory. In statistical analyses, participants were divided into two groups based on self-reported methamphetamine use in the month prior to assessment.

**Results:** Comparisons of the methamphetamine use groups, current users ( $n = 124$ ) and abstinent ( $n = 285$ ) indicate that those who abstained from using methamphetamine for the last month performed significantly better than those who used any methamphetamine in the last month on tests of working memory such as the Digit Symbol test and Trails B (both  $p < .05$ ).

**Conclusions:** Contrary to findings from prior studies, the performance of the groups on other neurocognitive tests did not statistically differ.

**Support:** This study was funded by CSAT contract #270-01-7089.

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**BEYOND ABSTINENCE: CAN COGNITIVE BEHAVIORAL THERAPY REDUCE CANNABIS-RELATED PROBLEMS?**

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**Aims:** Cannabis use disorders (CUD) are associated with many psychosocial problems. Treatment programs usually focus on abstinence as primary outcome measure but it is unclear to what extent they reduce cannabis-related problems. To resolve these problems can be necessary to achieve and maintain abstinence. It was hypothesized that, 10 sessions of combined Motivational Enhancement Therapy (MET), Cognitive Behavioral Therapy (CBT) and Psychosocial Problem Solving (PPS) (CANDIS, Hoch et al., 2007) lead to a significant reduction in cannabis-related problems in adolescents and adults with CUD (DSM-IV). No reduction was expected in the Delayed Treatment Control Group (DTC).

**Methods:** In a randomized controlled trial cannabis-related problems of  $N = 122$  subjects [Active Treatment (AT),  $n = 90$ , DTC,  $n = 32$ ] were assessed before treatment ( $t_0$ ), at post treatment ( $t_1$ ) and in a three and six months follow-up ( $t_2$  &  $t_3$ ). For the measurement of cannabis-related problems a German version of the 19 item Marijuana Problem Scale (MPS; Stephens et al., 2000) was used. A global problem severity index for each assessment time was build. Treatment effects were determined using repeated measures ANOVA.

**Results:** Cannabis-related problems were significantly reduced in the AT at post treatment [ $F(1, 77) = 88.60, p < .001, \eta^2 = .52$ ]. This effect was stable at three month follow-up [ $F(1, 61) = 20.80, p < .001, \eta^2 = .25$ ] and six month follow-up [ $F(1, 53) = 24.78, p < .001, \eta^2 = .32$ ]. No pre-treatment differences in frequency of cannabis-related problems could be found between AT and DTC [ $F(1, 118) = 0.002, n.s.; 1-\beta = .88$ ]. At post-treatment AT-DTC-differences were significant [ $F(1, 106) = 21.40, p < .001, \eta^2 = .17$ ].

**Conclusions:** The multi-component intervention CANDIS is effective in reducing cannabis-related problems. Further investigation is needed to analyze the relationship between problem reduction and abstinence and if there are problems that can be easier resolved than others.

**Support:** German Federal Ministry of Health, German Federal Ministry of Education and Research.

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**MU-OPIOID RECEPTOR A118G POLYMORPHISM IN HEALTHY VOLUNTEERS AFFECTS HPA-AXIS ACTH STRESS RESPONSE TO METYRAPONE.**

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**Aims:** To determine whether the A118G polymorphism in the mu opioid receptor affects hypothalamic-pituitary-adrenal axis response to metyrapone.

**Methods:** Healthy, normal volunteer subjects were recruited from ongoing genetics studies at Rockefeller University. Subjects received medical and psychiatric evaluations prior to being admitted to an inpatient unit at Rockefeller University Hospital. Written informed consents, specific for both genetics and inpatient neuroendocrine testing were obtained from each subject. On the test day, blood was sampled from 10 minutes prior to administration of a standard dose of oral metyrapone, 2.25gm, up to 8 hrs afterward; plasma levels of ACTH and cortisol were assayed. Three timepoints were used in analyses of the ACTH response to metyrapone: time 0, 4 hr and 8 hrs after administration.

**Results:** A total of 89 normal, healthy volunteers participated (32 women), 73 with the prototype AA genotype and 16 with one copy of the 118G allele in exon 1 of the mu-opioid receptor. A 3-way ANOVA of ACTH, Genotype X Gender X Time, showed a significant Genotype X Time interaction,  $p < 0.05$ . Although there was no basal difference, people with the AG genotype had significantly lower plasma ACTH than those with the prototype AA at the 8-hr time point. Two-way ANOVA of each genotype showed no main effect of gender, but in the AA genotype, ACTH levels were higher at 8 hrs in females than in males, and this was not found in the AG genotype. These findings suggest a relatively greater inhibition at the hypothalamic and anterior pituitary sites by the mu-opioid receptor tonic inhibition and relatively less cyclical glucocorticoid inhibition in those with the 118G allele.

**Conclusions:** The single nucleotide polymorphism A118G of the mu opioid receptor affects ACTH response to metyrapone, with subtle gender differences.

**Support:** NIH-NIDA P60-DA005130 (M.J.K) and RR UL1RR024143 (B.C.)

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### PRELIMINARY FUNCTIONING OUTCOMES OF A BEHAVIORAL TREATMENT TRIAL IN OPIATE IDU IN UKRAINE.

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**Aims:** The aim of this randomized standard treatment-controlled trial is to test the efficacy of a transported behavioral intervention for opiate injection drug users (IDU) in central Ukraine on drug abstinence and functioning outcomes.

**Methods:** This report is a preliminary analysis for 116 subjects with 13 months follow-up (range = 70-91%). The sample was recruited from IDU entering addiction treatment at the Vinnitsya Regional Narcological Dispensary (VRND). The experimental intervention was behavioral day treatment + standard inpatient medical care, with 3 months aftercare including therapeutic goal management with vouchers. Subjects were assessed at 1, 4, 7 (2nd point) and 13 (3rd point) months post treatment entry using Addiction Severity Index (ASI), Beck Depression Inventory (BDI), and Brief Symptom Inventory (BSI). Changes in scores were compared using Student's t-test with Satterthwaite extension.

**Results:** No baseline differences between groups were found for ASI drug score or psychiatric status or BSI score. Both groups showed reduction in severity on the drug score at follow-up. The change was greater for experimental vs control group at 2nd and 3rd points (-0.15 points vs -0.08,  $p=0.02$  at 2nd; -0.17 vs 0.07,  $p=0.001$  at 3rd). The experimental group showed improvement in psychiatric status at both points, but controls worsened (-0.06 vs +0.02,  $p=0.08$ ; -0.16 vs +0.01,  $p=.001$ ). Baseline ASI family/social functioning was worse in experimental vs control group (0.62 vs 0.47,  $p=0.008$ ). But the experimental group showed greater improvement at 3rd point (-0.23 vs -0.07,  $p=0.04$ ). Psychological distress (BSI) decreased more in the experimental vs control group at 2nd and 3rd points (-0.67 vs. -0.23,  $p=0.002$ ; -0.76 vs -0.30,  $p=0.002$ ).

**Conclusions:** Behavioral treatment affects drug abuse and other areas of life functioning at VRND.

**Support:** This project is funded by U.S. National Institute on Drug Abuse grant # 5R01DA18240.

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### RANDOMIZED CONTROLLED TRIAL USING CONTINGENCY MANAGEMENT TO PROMOTE SMOKING ABSTINENCE AMONG OPIOID-MAINTAINED PATIENTS.

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**Aims:** Prevalence of cigarette smoking among opioid-maintained (OM) patients is more than 3-fold that of the general population and associated with increased morbidity and mortality. This study evaluated the feasibility of using contingency management (CM) to reduce smoking in OM patients.

**Methods:** Forty methadone- or buprenorphine-maintained participants visited the clinic daily for the 14-day intervention. To be eligible, participants had to report smoking  $\geq 10$  cigarettes a day for  $\geq 1$  year, had a stable opioid maintenance dose and had a low occurrence of illicit drug abuse in the past 30 days. While not a primary focus, participants interested in pharmacotherapy could also receive bupropion (Zyban®). Participants provided breath and urine samples at each visit. Abstinence was defined on Days 1-5 as a breath carbon monoxide (CO) level  $\leq 6$  ppm and on Days 6-14 as a urine cotinine value  $\leq 80$  ng/ml. Contingent participants ( $n=20$ ) earned voucher-based incentives contingent on smoking abstinence (maximum earnings \$362.50), while Noncontingent participants ( $n=20$ ) received vouchers independent of smoking status.

**Results:** Participants were 33% male, 88% Caucasian and 31+ 7.7 years old. Contingent participants achieved significantly more smoking abstinence than Noncontingent (76% vs. 29% negative samples, respectively;  $p<.01$ ) and longer durations of continuous abstinence (10.7 vs. 4.1 days;  $p\leq.01$ ). There was no effect of bupropion on outcomes. Finally, there was a trend toward more smoking abstinence among Contingent participants at follow-up, though this did not meet statistical significance.

**Conclusions:** Results from this randomized clinical trial demonstrate the efficacy of CM in promoting smoking abstinence in this hard-to-treat population. Furthermore, considering that opioid treatment clinics throughout the country adhere to a relatively uniform set of guidelines, there is potential for wide dissemination of this intervention to treatment programs nationwide.

**Support:** National Institute on Drug Abuse T32 DA007242 and R01 DA019550

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### RACIAL DISPARITIES IN RESIDENTIAL SUBSTANCE ABUSE TREATMENT PROGRAMS.

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**Aims:** Understanding the role of race in the success of residential substance abuse treatment facilities is essential to improving the effectiveness of treatment for all clients. The aim of the current study is to examine the effect of race on client engagement in treatment, comparing client racial differences in treatment engagement by racial composition of the treatment program.

**Methods:** Data were collected on a national sample of 67 treatment programs (38 majority black and 29 majority white) using the Multimodality Quality Assurance Instrument to assess a wide range of organizational, program treatment, and client characteristics.

**Results:** Results show that black clients scored lower than whites in treatment engagement ( $p<.05$ ), and that the racial composition of programs was a significant predictor of client engagement in treatment ( $p<.008$ ), with majority white programs evincing significantly higher levels of client engagement in treatment ( $p<.008$ ). However, when blacks were compared to whites within the same programs, blacks had higher levels of engagement than whites regardless of program racial composition status.

**Conclusions:** The results suggest that differences between majority black and majority white programs resulted from programmatic rather than racial effects. This conclusion is reinforced by additional analyses, which showed that, when organizational characteristics associated with client engagement were added to the original mixed model, program race was no longer a significant predictor of client engagement ( $p=0.928$ ). These results indicate that, while black clients had lower levels of treatment engagement overall, the differences appeared to be program, not racial, effects.

**Support:** Behavioral Science Training in Drug Abuse Research, Public Health Solutions T32DA007233; NIDA grant (R01 DA015264) awarded to CIRP/NDRI.

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### COST OFFSET ANALYSIS OF AN ENHANCED HIV INTERVENTION FOR RURAL PROBATIONERS.

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**Aims:** Rural individuals experience unique barriers with regard to managing various types of risky behaviors (Leukefeld Edwards, 1999). The funding of HIV interventions is of primary importance to reducing societal costs and improving individuals' health, especially among people living in rural areas who are also involved in the criminal justice system. The purpose of the current study was to explore the cost offset of a standard vs. enhanced intervention for HIV risk behaviors, particularly focusing on those behaviors related to substance abuse.

**Methods:** 800 participants were recruited in probation offices within 30 rural counties in Kentucky. The mean age of participants was 32.2 years. The sample was primarily unmarried (70.6%), white (94.4%), and male (71.3%) with an average of 1.9 children. Two waves of data were gathered across a 6-month interval. Cost information was obtained from project budget records.

**Results:** Primary cost analyses were conducted using an adapted form of the Drug Abuse Treatment Cost Analysis Program (French, Dunlap, Zarkin, et al., 1997). Results indicated that although costs involved in administering the enhanced intervention were higher, participants who completed the program reported significantly less post-intervention drug abuse treatment costs. More specifically, along with reduction in risk behavior, individuals given the enhanced intervention accumulated approximately \$34.00 less in substance abuse treatment costs per dollar spent on their intervention than did participants in the standard intervention ( $B=-34.04$ ,  $SE=14.24$ ,  $p<.05$ ).

**Conclusions:** Given the scarcity of resources available to create effective treatment environments in rural areas, it has become even more critical to utilize existing funding efficiently with regard to planning and implementing risk reduction programs. Results suggest that creating an intervention tailored to the specific needs of rural at-risk populations can be both beneficial and cost effective in altering risk behavior in rural probationers.

**Support:** This research was supported by the National Institute on Drug Abuse (R01-DA11580).

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**THE PROVISION OF DRUG COUNSELING SERVICES IN OFFICE-BASED BUPRENORPHINE TREATMENT.**

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**Aims:** Drug counseling can improve outcomes in office-based treatment of opioid dependence. However, office-based physicians have historically had limited involvement with substance abuse treatment; the extent to which they can provide or access counseling is unknown. The purpose of our study was to investigate counseling practices among buprenorphine (BPN) prescribing physicians and assess perceptions of patient need and access to services.

**Methods:** We recruited novice and experienced BPN prescribers through the Physician Clinical Support System; physicians located in states with the highest prevalence of opioid abuse were eligible to participate. Using a web-based survey (N=195), we assessed provision of counseling services; types/locations of services; and perceived barriers. We then conducted in-depth qualitative interviews (N=33) to further investigate perspectives on need for and access to counseling.

**Results:** The sample includes physicians with a range of specialties and addiction experience working in a variety of practice settings. Most physicians believed counseling to be important adjunct to BPN, which was most often provided on-site by physicians (30%) or other staff (31%). About a quarter (24%) reported usually providing off-site referrals. The most significant barriers to counseling were affordability (mean=6.0/10-pt scale); public (6.1) and private insurance restrictions (5.6); and lack of patient interest (5.9). Other barriers mentioned were lack of physician time and addiction-related stigma. Despite these barriers, physicians overwhelmingly supported the integration of BPN, medical care, and counseling.

**Conclusions:** Findings suggest that many physicians attempt to link BPN prescribing and counseling; however, financing and patient acceptance are important barriers. A range of education and policy strategies are needed to assist physicians, including training and guidelines for providing counseling/referrals; improved systems for integrating/linking BPN and counseling; and addressing financing barriers to assure coverage.

**Support:** Funded by RWJF grant#61231.

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**CHANGES IN PREGNANOLONE DISCRIMINATIVE STIMULUS AS A FUNCTION OF TRAINING DOSE IN RATS.**

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**Aims:** Neuroactive steroids (NAS) can positively modulate GABAA receptors. A growing body of evidence suggests that the discriminative stimulus effects of NAS involve multiple mechanisms of action. Training dose can be an important consideration for drugs with multiple mechanisms of action given that substitution profiles in drug discrimination studies are influenced by training dose, including the potency and selectivity of test compounds.

**Methods:** The present study compared different training doses of pregnanolone in separate groups of male Sprague-Dawley rats (n=8 per group) discriminating pregnanolone from vehicle and responding under a two-lever FR10 schedule of food presentation. To determine the smallest and largest reliably discriminable doses, two groups were initially trained to discriminate 3.2 mg/kg pregnanolone (i.p.) which was systematically either decreased to 1.33 or increased to 7.5 mg/kg.

**Results:** Decreasing the training dose to 1.33 mg/kg yielded an ED50 of 0.55 mg/kg and increasing the training dose to 7.5 mg/kg yielded an ED50 of 2.20 mg/kg. There were no differences in response rates between groups. In addition, the benzodiazepines midazolam and flunitrazepam produced >80% drug-lever responding in all rats, while morphine produced predominantly vehicle-lever responding.

**Conclusions:** These results suggest that altering the training dose changes the sensitivity of the discriminative stimulus effects of pregnanolone and may provide a framework for studies that could elucidate the multiple mechanisms of action of NAS.

**Support:** Supported by DA017240.

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**VALPROIC ACID ATTENUATES ACUTE AMPHETAMINE-INDUCED LOCOMOTION IN MICE.**

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**Aims:** D-Amphetamine is known to increase extracellular dopamine levels by stimulating its release from synaptic terminals. Valproic acid, an anticonvulsant and mood-stabilization agent, increases GABA levels and inhibits glycogen synthase 3 (GSK3), a suspected modulator of dopamine-dependent behaviors. Previous studies from our laboratory indicate that mice pretreated with valproic acid display a dose-dependent attenuation of acute cocaine-induced locomotor activity. Here, we investigated the effect of valproic acid on amphetamine-induced hyperactivity in mice.

**Methods:** Adult male CD-1 mice were pretreated with saline or valproic acid (50-300 mg/kg, i.p.) 30 minutes prior to an amphetamine challenge (2.0 mg/kg, i.p.) and locomotor activity was measured for 60 minutes.

**Results:** Mice pretreated with valproic acid (300 mg/kg) exhibited a significant attenuation of amphetamine-induced ambulatory activity and stereotypic activity as compared to saline-pretreated amphetamine controls.

**Conclusions:** These data demonstrate that valproic acid attenuates amphetamine-induced hyperactivity. Future studies will examine the effects of valproic acid on amphetamine-induced locomotor sensitization and conditioned place preference. The role of GSK3 in amphetamine-induced behaviors will be further investigated using the selective GSK3 inhibitor, SB 216763.

**Support:** Supported by DA 09580 (EMU)

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**PHARMACOKINETICS OF LISDEXAMFETAMINE DIMESYLATE FOLLOWING INTRANASAL ADMINISTRATION.**

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**Aims:** To compare the pharmacokinetics of d-amphetamine derived from lisdex-amfetamine dimesylate (LDX) after single intranasal (IN) and oral (PO) doses of LDX.

**Methods:** This single-center, randomized, open-label, 2-period, crossover study enrolled 18 healthy adult males (18 to 65 years). Subjects received LDX 50 mg solution radiolabeled with up to 100  $\mu$ Ci <sup>99m</sup>Tc-DTPA IN and LDX 50 mg capsule PO at  $\geq$ 7-day intervals. IN administration was confirmed by scintigraphy. Blood was drawn for d-amphetamine and LDX levels predose, 15, 30, 45 minutes and 1, 1.5, 2, 3, 4, 5, 6, 8, 12, 16, 24, 36, 48, and 72 hours after IN or PO administration and additionally at 5, 10, and 20 minutes after IN dosing. Treatment-emergent adverse events (TEAEs) were assessed.

**Results:** Following IN LDX, the mean (SD)  $C_{max}$ ,  $AUC_{last}$ , and  $AUC_{inf}$  of d-amphetamine were 35.9 (6.49) ng/mL, 690.5 (157.05) ng•h/mL, and 746.2 (171.58) ng•h/mL, respectively. After oral LDX, the mean (SD)  $C_{max}$ ,  $AUC_{last}$ , and  $AUC_{inf}$  of d-amphetamine were 37.6 (4.54) ng/mL, 719.1 (157.05) ng•h/mL, and 776.9 (167.69) ng•h/mL, respectively. Median  $T_{max}$  and mean (SD)  $t_{1/2}$  were similar between the 2 routes of administration (4 [IN] vs 5 [PO] hours for  $T_{max}$ ; 11.3 (1.8) [IN] vs 11.6 (2.8) [PO] hours for  $t_{1/2}$ ). The incidence of TEAEs was higher after IN (7 of 18 subjects: 38.9%) than PO administration (5 of 18 subjects: 27.8%). TEAEs were consistent with the known effects of amphetamines. Most were mild and none was severe.

**Conclusions:** IN and PO administration of LDX resulted in equivalent exposure to d-amphetamine concentrations. The rate and extent of d-amphetamine exposure were similar for both routes of administration. Thus, when LDX is administered IN, the bioavailability of d-amphetamine is not increased compared with PO. Safety profiles after PO and IN LDX were similar.

**Support:** Supported by funding from Shire Development Inc.

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### NICOTINE OCCUPANCY OF BETA2\*-NICOTINIC ACETYLCHOLINE RECEPTORS AFTER USE OF NICOTINE INHALER: RELATIONSHIP TO CRAVING.

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**Aims:** The nicotine inhaler aims to reduce craving by mimicking cigarette's behavioral component and delivering controlled doses of nicotine without the harmful tars. However, the pharmacokinetics of nicotine after use of the inhaler are different from a cigarette, and the arterial nicotine level spike seen after use of cigarettes is absent with use of inhaler. We aimed to measure nicotine occupancy of beta2\*-nicotinic acetylcholine receptors (nAChRs) after use of a nicotine inhaler, and the relationship to reduction in cigarette craving.

**Methods:** Nine abstinent (6.9±1.5d) control smokers (age=36.1±12.9y; 4men, 5women) participated in [123-I]5IA SPECT imaging and nicotine inhaler challenge. Subjects used the inhaler every 15sec for 20min. Arterial (up to 30min) and venous (60-300min) plasma nicotine levels were collected post initiation of challenge. Assessments of nicotine craving (Tiffany Questionnaire of Smoking Urges) and withdrawal (Minnesota Withdrawal Questionnaire) were administered pre/post challenge.

**Results:** Use of the nicotine inhaler produced ~75% occupancy of beta2\*-nAChR in cortical regions, thalamus, striatum, and cerebellum, with 364.7±125.8ng of plasma nicotine concentration over 60min. Comparison of pre to post scores revealed a significant decrease in self-reported withdrawal symptoms post nicotine inhaler ( $t=3.4$ ,  $p<.01$ ), but not desire and expected relief. However, we observed a significant positive association between reported desire for cigarette after use of inhaler and occupancy of beta2\*-nAChR in the cerebellum ( $p=.05$ ), as well as nonsignificant positive trends in parietal, temporal, and occipital cortices and striatum (all  $p<.1$ ).

**Conclusions:** Results suggest that after use of nicotine inhaler, occupancy of beta2\*-nAChR is similar to smoking a single cigarette and the amount of occupancy positively correlates with the desire to smoke a cigarette.

**Support:** RO1DA015577, R21 DA020788, P50AA15632, KO2DA021863.

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### SERVICE NEEDS, TREATMENT UTILIZATION, AND OUTCOMES OF ASIAN AMERICANS IN DRUG TREATMENT.

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**Aims:** To examine differences in substance abuse treatment needs, treatment utilization, and outcomes between Asian Americans/Pacific Islanders (AAPI) and others.

**Methods:** Secondary analysis was conducted on data collected by two studies of patients admitted to community-based drug treatment in three states (California, Hawaii, & Montana) that utilized the same standardized measures at three observation points over a one-year period from treatment intake to 12-month follow-up. Data were analyzed on 298 AAPI and a sample of 298 non-AAPI matched on gender, age, primary drug problem, and treatment program. Differences in pretreatment characteristics, treatment retention, treatment completion, and outcomes were examined.

**Results:** At treatment entry, about two-thirds of the sample reported methamphetamine as the primary drug problem, most had experienced one prior drug treatment despite an average of 12 years of use, half reported psychiatric problems, and one-third had been incarcerated recently. More AAPI than non-AAPI had used drugs in the 30 days prior to treatment entry (85.5% vs. 79.4%) and more AAPI reported smoking as the primary method for using drugs (82.3% vs. 66.4%). According to problem severity composite measures, AAPI entered treatment with less severe alcohol and medical problems than non-AAPI and similarly severe problems in other domains. Compared to non-AAPI, AAPI reported better general health and less desire for services to address alcohol and medical problems. There were no group differences in rates of treatment retention or completion. Treatment outcomes were similar between the two groups, with AAPI demonstrating better outcomes in the alcohol, family, and medical domains.

**Conclusions:** Despite cultural protective factors, AAPI have similar service needs, rates of treatment utilization, and outcomes as other racial/ethnic groups in drug treatment.

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### DRUG MARKET ACTIVITY INFLUENCE ON ADOLESCENT SCHOOL CONDUCT.

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**Aims:** Previous research suggests a relationship between social disorganization factors negative outcomes for adolescents. However, it is not known what extent individual indicators of social disorganization contribute to individual adverse outcomes. The present study examined specificity in relationships among neighborhood social disorganization factors and adolescents' school conduct. In particular we examined the independent influence of the presence of drug dealers in the community on students' school conduct. We hypothesized after controlling for traditional neighborhood indicators (e.g., perceived poverty and trash/broken bottles) an association between youths' school conduct and perception of neighborhood drug dealing would emerge.

**Methods:** Data was collected as part of a large study evaluating the efficacy of drug abuse prevention in middle school youth. The present study included 210 adolescents aged 11 to 16. The sample was evenly split by gender and 80% black. Stepwise logistic regression analysis was employed to examine the influence of three social disorganization measures on youths' school conduct.

**Results:** On Step 1, no significant relationship emerged between physical environment and school conduct while controlling for demographic factors. On Step 2, while controlling for demographic factors and physical environment, no relationship emerged between perceived poverty and school conduct. On the final step, a significant relationship emerged between neighborhood drug dealing and school conduct (OR= 1.9; 95%CI= 1.04, 3.52).

**Conclusions:** The findings suggest the presence of drug markets influences adolescent behavior independent of other social disorganization indicators. It may be that perceiving drug dealers as the money makers diminishes the value of education or respect for school evident in acting out. Future research should focus on identifying drug market hot spots and designing interventions for students living in these areas who may be at greater risk than those living in deprived or disorganized areas free of drug dealers.

**Support:** NIDA R01 DA015075 and NIDA Epidemiology Training Program 2T32DA007292

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### EMPLOYMENT-BASED REINFORCEMENT OF ADHERENCE TO DEPOT NALTREXONE PHARMACOTHERAPY.

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**Aims:** Naltrexone is an opiate antagonist that is pharmacologically effective but of limited clinical utility because of problems with medication compliance. Extended-release depot naltrexone injections provide effective blockade for up to four weeks. Concurrent behavioral treatment could promote adherence to the depot treatment and thus significantly enhance its clinical utility. This study investigated the effectiveness of employment-based reinforcement in increasing acceptance of depot naltrexone injections.

**Methods:** Participants were unemployed heroin-dependent adults who worked at a therapeutic workplace and earned vouchers each weekday for 26 weeks. Participants were prescribed one depot naltrexone injection every 3 weeks throughout the first 15 weeks. Participants were randomly assigned to either a Naltrexone Contingency ( $n = 18$ ) or Naltrexone Offered ( $n = 17$ ) group. Those in the Contingency group could only work if they accepted the depot injections. Those in the Offered group could work regardless of whether they accepted the injections.

**Results:** Eighty-one percent of the injections were accepted by participants in the Contingency group, whereas 42% of the injections were accepted by participants in the Offered group. The difference between the groups was statistically significant ( $p = .008$ ; OR = 5.68). During the first four months (the period covered by the depot naltrexone), opiate use was low in both groups. Approximately 88% and 76% of the urine samples were negative for opiates in the Contingency and Offered groups, respectively. The difference in opiate-negative urine samples was not significant. Among all participants, there was a significant correlation between the percentages of accepted depot injections and opiate-negative urine samples ( $r_s = .51$ ;  $p = .003$ ).

**Conclusions:** Employment-based reinforcement can increase adherence to depot naltrexone pharmacotherapy. Although opiate use was low in both groups, there was a positive correlation between the percentages of depot injections accepted and opiate-negative samples.

**Support:** NIDA Grants R01DA019497 and T32DA07209

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**MEDICAL CARE UTILIZATION AND OPIATE DEPENDENCE.**

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**Aims:** When compared to the general population, substance abusers experience more medical problems (Mertens et al., 2005). Primary care physicians, trauma centers, emergency rooms, and other clinics should consider regularly performing substance abuse screening and brief intervention (SBI) since drug and alcohol use puts individuals at risk. Although it helps to decrease drug use (Madras et al., 2008), the extent to which SBI is implemented in healthcare settings remains unclear.

**Methods:** During the screening phase of a continuing NIDA-funded trial comparing the effectiveness of combined pharmacotherapy and behavioral therapy for opiate dependence, participants are asked about their medical care to investigate whether a substance use discussion or assessment occurred.

**Results:** Preliminary results for the first 140 participants indicate that 77% have seen a doctor or other healthcare professional in the 12 months prior to the study screening. Of the participants who attended a medical visit, 44% reported that they initiated a discussion of drug and/or alcohol use, while only 22% of healthcare providers initiated such a discussion. Although the majority of the sample engaged in a discussion of substance use with their healthcare provider, less than half (43%) reported that they were given a drug and/or alcohol use assessment.

**Conclusions:** These results have important implications in that they show that opiate users do utilize medical care and even discuss their substance use with their primary care providers; however few are given the substance use assessments that may help to identify and address drug problems. Other findings about drug and alcohol use assessments in primary care settings are provided and discussed.

**Support:** NIDA grant #DA020210.

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**QUALITY OF LIFE AND SEVERITY OF PROBLEMS RELATED TO ALCOHOL MISUSE.**

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**Aims:** This study assesses the impact of problems related to alcohol misuse in quality of life (QOL).

**Methods:** A cross-sectional multi-center sample of 300 current adult substance abusers from outpatient and inpatient clinics was collected by three research centers located in Brazilian state capitals. From this sample, 174 subjects were selected for the study as they reported that they sought treatment due to the problems caused by alcohol misuse. All of them had problems with alcohol use in the last 30 days. The WHOQOL-BREF was used to measure QOL, and the sixth version of the Addiction Severity Index (ASI6) to investigate the severity of problems related to alcohol and substance use. The main outcomes measures included in the linear regression analyses were the domains of WHOQOL-BREF, the independent factors were the areas of ASI score, and the potentials confounding factors such as age, gender and schooling.

**Results:** The average age of the sample was 40 years and 87% of the subjects were male. Sixty seven percent of them did not graduate from high school and 65% were unemployed. The average years of alcohol use and abuse were 15 and 11, respectively. Negative correlations were showed between many of the ASI composite scores and the WHOQOL-Bref domains. In addition, ASI Medical area was associated to lower scores in all WHOQOL domains and ASI psychiatric area to psychological (-0.6) and physical (-0.5) areas. Employment problems were also associated to low scores in the physical and environmental (-0.3 for both) and family problems to social (-0.7) and environmental (-0.5) domains.

**Conclusions:** Our results points to a broad negative impact of the severity of alcohol misuse in QOL. Treatment and interventions should not only be focused on reducing substance use in alcoholics but also address these other problems in order to significantly improve QOL in this population.

**Support:** This study was supported by National Secretariat for Drug Policy (SENAD).

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**CAUSES OF DEATH AMONG CRACK USERS IN MIDWESTERN AMERICAN CITY.**

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**Aims:** The use of crack cocaine has been linked to a range of social, psychological, and medical problems. Nevertheless, aside from case reports, there is little research on mortality among crack users in the United States. This study examined causes of death among a community sample of 430 crack smokers in the Dayton, Ohio, area.

**Methods:** A targeted sampling plan was used to recruit people 18 years of age or older to participate in a natural history of crack cocaine use and health services utilization. All participants tested positive on urinalysis for recent cocaine use at entry into the study. Participants were interviewed periodically between 1996 and 2005 by project staff using structured questionnaires. County death records were searched to identify individuals who had participated in the study.

**Results:** By the end of 2006, 36 (8.4%) participants had died. Most of the deceased were men (58.3%), African American (52.8%), and those with less than a high school education (63.9%). Women and whites were disproportionately represented. On average, approximately 14 years had elapsed between the self-reported initiation of crack use and the actual date of death. Death certificate data showed drugs were a contributing factor to death in 12 cases; cocaine was specifically mentioned in 4 cases. Violence was listed as the cause of death in 7 cases. Accidents accounted for 3 deaths and medical conditions in the remaining 14 cases.

**Conclusions:** Virtually all of the medical conditions recorded on the death certificates could have been related to drug use, e.g. cardiac arrest due to hypertensive cardiovascular disease, cirrhosis due to hepatitis C. This study's limitations are likely to have contributed to an under-counting of deaths in the sample.

**Support:** This research was supported by NIDA Grant # R01DA010099.

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**TOLERANCE DEVELOPMENT TO HALLUCINOGEN-ELICITED HEAD TWITCH BEHAVIOR IN MICE.**

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**Aims:** Hallucinogenic drugs with agonist affinity at serotonin 5-HT<sub>2A</sub> receptors elicit a characteristic head twitch response in mice which has been argued to represent a selective murine model for hallucinogen-like drug effects. In humans, repeated administration of hallucinogens is known to blunt the subjective effects of these drugs, but the consequences of repeated drug exposure on expression of head twitch behavior in the mouse are largely uncharacterized.

**Methods:** In these studies, adult male Swiss Webster mice were injected with various doses of the phenethylamine hallucinogen 2,5-dimethoxy-4-iodoamphetamine (DOI) or the tryptamine hallucinogen dipropyltryptamine (DPT) to generate dose-effect relationships for these compounds on head twitch behavior. Behaviorally-equivalent doses of DOI and DPT, or saline vehicle, were then repeatedly administered every 24 or 48 hours, for 5 total injections, and head twitch behavior was quantified.

**Results:** Repeated injections of DOI resulted in a progressively blunted head twitch response, and the development of this tolerance was more rapid when DOI was injected every 24 hours than when it was injected every 48 hours. In contrast, repeated DPT administration did not result in tolerance development, regardless of the inter-injection interval.

**Conclusions:** These findings further underscore the differences between phenethylamine- and tryptamine-based hallucinogens in animal models, and may suggest important distinctions in their drug-receptor interactions. Further pharmacological implications of these data will be discussed.

**Support:** These studies supported by USPHS grants DA020645 and RR020146.

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**THE IMPACT OF DIRECTIVE AND NON-DIRECTIVE DRUG COUNSELING APPROACHES AS A FUNCTION OF PATIENT TRAIT REACTANCE.**

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**Aims:** To test the differential impact of directive and non-directive counseling approaches for stimulant users scoring high or low on trait reactance.

**Methods:** 250 patients who successfully completed the Outpatient Matrix Model of stimulant abuse treatment were randomly assigned to one of five after-care counseling conditions: (1) unstructured/non-directive, (2) unstructured/directive, (3) structured/non-directive, (4) structured/directive, or (5) standard referral to aftercare without telephone counseling (control). The two structured conditions are based on the behavioral "prompts" identified by Farabee et al. (2002) as being associated with drug avoidance. In the non-directive conditions, pts state their own goals and how they intend to achieve them. In the directive conditions, the counselor provides specific recommendations for the adoption of as many drug-avoidance activities as possible.

**Results:** A call satisfaction survey administered at the 3-month follow-up revealed that, overall, subjects tended to be more satisfied with the directive conditions (unstructured directive and structured directive), as well as having higher agreement scores with the statement that the calls increased their participation in drug avoidance activities. Satisfaction levels were not associated with the structure of the interventions. Results provide partial support for the hypothesized interaction between the directiveness of the counseling style and the level of the patients' trait reactance. Although both low- and high-reactance subjects in the directive conditions were less likely to use stimulants than those in the non-directive conditions, the directive approaches were more effective for subjects scoring low on trait reactance.

**Conclusions:** This study provides evidence that matching drug counseling styles (directive versus non-directive) to patients' level of trait reactance can further enhance drug use and related outcomes.

**Support:** These findings were derived from a larger project entitled "Four Models of Telephone Support for Stimulant Recovery," which is funded by the National Institute on Drug Abuse (DA18208).

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**SEX DIFFERENCES IN NICOTINE SELF-ADMINISTRATION AND REINSTATEMENT IN RATS.**

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**Aims:** Nicotine addiction constitutes a substantial worldwide health issue that is particularly detrimental to women's health. However, traditional smoking-cessation programs result in poorer outcomes in women, an effect that may be related to gender differences in factors mediating nicotine addiction. Despite these issues, very little research has been devoted to ascertaining sex differences in ongoing nicotine-taking, as well as nicotine-seeking behaviors following exposure to various stimuli that contribute to relapse (e.g., conditioned cues, stress, and nicotine exposure). Thus, we examined sex differences in nicotine self-administration and reinstatement in rats.

**Methods:** Male (n=24) and female (n=40) Sprague-Dawley rats were trained to lever press for intravenous nicotine (0.05 mg/kg/infusion) paired with the presentation of a light+tone stimulus for 15 days. Once responding was extinguished in the absence of nicotine reinforcement, the ability of nicotine-paired cues, the anxiogenic  $\alpha$ 2-noradrenergic receptor antagonist, yohimbine (2.5 mg/kg, IP, alone and in combination with the nicotine-paired cues), and a priming injection of nicotine (0.5 mg/kg, IP) were examined for their ability to reinstate nicotine-seeking behavior.

**Results:** Both males and females readily acquired nicotine self-administration and displayed comparable levels of responding and nicotine intake during the maintenance phase. While yohimbine alone resulted in reinstatement of nicotine-seeking ( $p < 0.05$ ), yohimbine pretreatment in combination with the cues resulted in a supra-additive effect ( $p < 0.01$ ), with no sex differences noted under either reinstatement condition. However, females exhibited greater conditioned reinstatement, while males exhibited greater nicotine-primed reinstatement ( $ps < 0.05$ ).

**Conclusions:** Given these differences in reinstatement behavior following exposure to various relapsing stimuli, our results suggest that a better understanding of sex differences in relapse to nicotine-seeking will facilitate the development of gender-specific treatment strategies and improve abstinence outcomes for female smokers.

**Support:** Supported by NIH grant P50 DA16511 and 1K12ZDH55885-01

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**ASSESSMENT OF ADDICTIVE BEHAVIOR AMONG THE ELDERLY: WHAT ABOUT "GERIATRIC ADDICTION"?**

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**Aims:** World Health Organization defines Old age over 65 years. In North-America and Europe, old age population increase. However, little is known about addiction behavior in this population.

**Objectives:** To assess the possible links between gerontology and addiction medicine through a theoretical analysis assessment and a literature review.

**Methods:** Current definitions of gerontology and addiction medicine were used to seek possible theoretical links and MEDLINE database was used for the literature search.

**Results:** Regarding the definitions, some risk factors could be underlined for the development of addiction among old subjects. Because some socio-economic data show that old age may be associated to some wealth in income and increased free time some subjects who never experienced addiction lifetime could develop a late onset addiction. Others who had addiction as adults could persist on their addiction behavior, either with the same substance (or activity) or switch to another one. The literature supported this theoretical approach. Several clinical cases were reported showing late onset addiction among old subjects. Other studies and case reports indicated the absence of spontaneous remission of adult onset addiction in the elderly.

**Conclusions:** Further studies are needed to assess addictive behavior among subjects aged 65 and over. Moreover, current or future prospective studies on addiction should assess participants over 65. It is possible that there will be an increase in old age addiction patients due to the increase in old age general population.

**Support:** UB2, INSERM IFR99, CHU, CHCP, PHRC, MILDT-INSERM

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**SUBSTANCE USE AND RISKY SEXUAL PARTNERS IN WOMEN WITH BORDERLINE PERSONALITY DISORDER.**

Ulrike Feske, N De Genna, T Angiolieri, M Gold, M Cornelius; University of Pittsburgh, Pittsburgh, PA

**Aims:** BPD is characterized by an increased risk for substance use disorder (SUD). Co-occurring BPD and SUD is associated with multiple sex partners, sex trading, and needle sharing, thereby increasing the risk for HIV. This is the first study to systematically examine the relationship between SUD and sexual partner characteristics in BPD. It is hypothesized that women with BPD have riskier sex partners than women without BPD, even when the effects of SUD diagnoses are controlled statistically.

**Methods:** The sample consisted of 196 women between the ages of 18 and 40 ( $M = 26.7$ ,  $SD = 6.54$ ). Of these, 103 women (52.5%) met DSM-IV criteria for BPD. The remaining 93 women met DSM-IV criteria for a current, non-psychotic Axis-I disorder. Participants were administered the SCID-I and II and a Timeline Follow-Back interview in which they described all sexual and substance use in the past 6 months. They were asked about sex partners who used intravenous (IV) drugs, male sex partners who had sex with men (MSM), and whether they had ever engaged in the sex trade in the last 6 months and in their lifetime.

**Results:** Analyses were conducted using logistic regression models, controlling for age, race, SES, and SUD. Cocaine, opioid, and polydrug use were associated with sex trading and having a sex partner who used IV drugs in the last 6 months. BPD did not predict sex trade in the last 6 months, but it was a predictor of ever engaging in the sex trade. BPD diagnosis did not predict ever MSM sex partners, but more severe BPD was a risk factor for ever MSM sex partners. There was an interaction of lifetime SUD and race on risk for having a MSM partner, such that White women with alcohol, cocaine, opioid, or polydrug use were at higher risk.

**Conclusions:** Although BPD was associated with risky sexual partners in bivariate analyses, it was not a risk factor for all risky sexual partner outcomes in regression analyses controlling for age, race, SES, and SUD. These findings suggest that the effects of BPD may be mediated by SUD, with implications for HIV prevention in this high risk population of women.

**Support:** Supported by grant DA020130.

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**IMPULSIVE DISINHIBITION IN ADOLESCENT SMOKERS AND NONSMOKERS.**

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**Aims:** Impulsivity is a multidimensional construct that is often linked to various forms of addiction, including cigarette smoking. Much of this research has been restricted to use of self-report measures rather than also including laboratory behavioral assessments of impulsivity. One type of impulsivity assessed in the laboratory, which has been extensively examined in various clinical contexts, is impulsive disinhibition. However, the link between disinhibition and cigarette smoking status has yet to be explored.

**Methods:** The current study examined behavioral disinhibition using the Go/Stop Task between adolescent smokers ( $n = 50$ ) and nonsmokers ( $n = 50$ ). A self-report measure of impulsivity (Barratt Impulsiveness Scale-11-Adolescent; BIS-11-A) also was included.

**Results:** The results indicated a significant smoking status  $\times$  gender interaction effect for Go/Stop Task ( $F = 11.338$ ,  $p < .001$ ). Male nonsmokers had significantly higher stop signal reaction times (i.e., more impulsive) than male smokers ( $p = .012$ ), female smokers ( $p = .030$ ), and female nonsmokers ( $p = .012$ ). Also, female smokers had significantly higher stop signal reaction times than female nonsmokers ( $p = .029$ ) and male smokers ( $p = .030$ ). There were no differences found between male smokers and female nonsmokers. There were no main effects for smoking status or gender for the Go/Stop Task. These findings indicate that male smokers performed less impulsively on a measure of disinhibition than both male nonsmokers and female smokers. For the BIS-11-A, there were no interaction effects between gender and smoking status, but there was a main effect of smoking status ( $F = 8.064$ ,  $p < .01$ ).

**Conclusions:** These results will be discussed in the context of possible gender specific nicotine effects on disinhibition, a finding not identified with a more general self report measure of impulsivity.

**Support:** NIDA R21 DA0204 23-02

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**CROSS-COUNTRY VARIATIONS IN ILLEGAL DRUG INVOLVEMENT AND DSM-IV CLINICAL FEATURES OF DRUG ABUSE IN THE AMERICAS.**

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**Aims:** Cross-country variations in drug involvement and associated problems can be illuminated using latent class modeling (LCM) of epidemiological field survey data. In this LCM research, we seek to understand cross-country variation in the clinical features of DSM-IV drug abuse as it occurs in each country under study, with male-female (M-F) variation as an exploratory issue.

**Methods:** Data are from the World Mental Health Surveys Initiative, with probability samples in Mexico ( $n=5,826$ ), Colombia ( $n=4,426$ ) and the USA ( $n=5,692$ ), and with a standardized interview schedule used to assess illegal drug involvement and five clinical features that tap the non-hierarchical DSM-IV 'drug abuse' criteria.

**Results:** With 2,939 illegal drug users in the USA, 496 in Colombia, and 513 in Mexico, the best-fitting LCM showed 4 classes with qualitatively similar loadings for the three countries, although one class (with 'recurrent hazard-laden drug use' as a primary feature) was country-specific. In the USA, females and males had indistinguishable 4-class latent structures.

**Conclusions:** Drug problem experiences in these three very different American countries share a remarkably similar latent class structure, and in the USA, the male-female latent class structures also are similar. Larger samples, with a greater number of female drug users, will be needed to study M-F variations in Mexico and Colombia.

**Support:** NIDA Awards R01DA016558, K05DA015799, D43TW05819. (WMH web site provides other support details.)

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**ROLE OF GABA<sub>A</sub> RECEPTOR SUBTYPES IN BENZODIAZEPINE SELF-ADMINISTRATION BY RHESUS MONKEYS.**

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**Aims:** Benzodiazepines are effective anxiolytics and hypnotics, but their clinical utility is limited by potential for abuse. Recent experimental evidence suggests that the reinforcing effects of benzodiazepines may be mediated by distinct GABA<sub>A</sub> receptor subtypes. The present study examined the role of  $\alpha 1$ - and  $\alpha 5$ -subunit-containing GABA<sub>A</sub> receptors in the reinforcing effects of the conventional benzodiazepine triazolam.

**Methods:** Rhesus monkeys were prepared with intravenous catheters and trained under a progressive ratio schedule of i.v. midazolam injection (0.03 mg/kg/injection). Test sessions were conducted by substituting various doses of triazolam (0.0001-0.03 mg/kg/injection) for midazolam, both alone and after pretreatment with subtype-preferring benzodiazepine site antagonists.

**Results:** When evaluated alone, triazolam availability resulted in an inverted "U" shaped dose-response function in all subjects, with peak doses of triazolam maintaining 10-14 injections per session. Pretreatment with the nonselective antagonist flumazenil (0.01-0.3 mg/kg, i.v.) reduced triazolam self-administration, with at least one dose of flumazenil attenuating the peak effects of triazolam in every monkey. Similar results were observed with the  $\alpha 1$  GABA<sub>A</sub> receptor-preferring antagonists  $\beta$ CCT (0.1-1 mg/kg, i.v.) and 3-PBC (0.3-3.0 mg/kg, i.v.). In contrast, pretreatment with the  $\alpha 5$  GABA<sub>A</sub> receptor-preferring antagonist Xli-093 (0.003-0.1 mg/kg, i.v.) did not attenuate the peak effects of triazolam.

**Conclusions:** Together, these data suggest a role for the  $\alpha 1$  GABA<sub>A</sub> receptor subtype, but not the  $\alpha 5$  GABA<sub>A</sub> receptor subtype, in the reinforcing effects of benzodiazepines.

**Support:** Supported by DA011792, AA16179, MH46851, RR00168

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**EVALUATION OF [<sup>3</sup>H]-SN56, A NOVEL SIGMA-1 RECEPTOR RADIOLIGAND.**

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**Aims:** Numerous studies have demonstrated that antagonism of the sigma-1 receptor attenuates the toxic and psychostimulant effects of cocaine and methamphetamine in animal models. Screening of new sigma-1 antagonists relies heavily on binding affinity determinations because there are no established functional assays available for sigma-1. The radioligand presently used for *in vitro* studies of sigma-1, [<sup>3</sup>H]-(+)-pentazocine, has significant limitations; it is difficult to synthesize, has limited chemical stability, and can be problematic to obtain. Evaluation of a series of novel compounds revealed SN56 to have unprecedented affinity and selectivity for sigma-1. The aim of this project was to characterize [<sup>3</sup>H]-SN56 as a potential replacement for [<sup>3</sup>H]-(+)-pentazocine in radioligand binding studies.

**Methods:** Standard *in vitro* filter binding techniques were utilized to: 1) determine the specificity and affinity of binding of [<sup>3</sup>H]-SN56 to sigma-1 receptors, 2) confirm that [<sup>3</sup>H]-SN56 labels sites previously identified as sigma-1 by comparing binding to sites labeled by [<sup>3</sup>H]-(+)-pentazocine, and 3) characterize the kinetics of [<sup>3</sup>H]-SN56 binding.

**Results:** The results of these studies indicate that [<sup>3</sup>H]-SN56 exhibits: 1) specific, saturable, and reversible binding to the sigma-1 receptor, with  $B_{max} = 340 \pm 10$  fmol/mg and  $K_d = 0.069 \pm 0.007$  nM, 2) competitive displacement by classical sigma compounds, yielding  $K_i$  values consistent with those reported in the literature, and 3) binding kinetics compatible with a 1.5 h incubation and filtration for separation of free from bound radioligand.

**Conclusions:** [<sup>3</sup>H]-SN56 appears to be a good candidate as a replacement for [<sup>3</sup>H]-(+)-pentazocine in radioligand binding assays. Further, because [<sup>3</sup>H]-SN56 has a >100-fold higher affinity for the sigma-1 receptor vs. [<sup>3</sup>H]-(+)-pentazocine, competition binding studies require less radioligand and membrane, resulting in significant efficiencies in resources when performing the assays.

**Support:** Funding for this work was provided by the National Institute on Drug Abuse (DA013978, DA023205).



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### METHAMPHETAMINE-RELATED VS COCAINE-RELATED EMERGENCY DEPARTMENT VISITS IN URBAN VS RURAL COUNTIES IN CALIFORNIA.

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**Aims:** Emergency Department (ED) utilization for cocaine-related problems in urban areas is well documented. Anecdotal reports suggest ED utilization for methamphetamine-related problems is common, but data is limited. We compared methamphetamine-related and cocaine-related ED visits in urban versus rural counties in California using a state-wide database of ED visits.

**Methods:** Methamphetamine-related and cocaine-related ED visits were abstracted via ICD-9 codes from the 2006 California Office of Statewide Health Planning and Development database of ED visits to all nonfederal hospitals in California. Age adjusted rates, demographics, and primary diagnoses for methamphetamine-related and cocaine-related ED visits in metropolitan, micropolitan, and rural counties were compared.

**Results:** There were 27,050 methamphetamine-related ED visits in California in 2006 compared to 15,558 cocaine-related ED visits. Methamphetamine-related ED visits were widespread throughout California, while cocaine-related ED visits were concentrated in a few urban counties. Rural and micropolitan counties accounted for four out of the top five counties with the highest per capita rate of methamphetamine-related ED visits.

**Conclusions:** Methamphetamine-related ED visits outnumbered cocaine-related visits in California. Rural and smaller suburban counties were disproportionately impacted by high rates of methamphetamine-related ED visits, yet substance abuse treatment/prevention services in these counties are limited. Increased funding and resources for methamphetamine treatment/prevention in rural and suburban counties are urgently needed.

**Support:** Funding for this study was provided by NIDA grants 1 K23 DA 023558 and 1 P50 DA 18185.

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### THE MODERATING EFFECTS OF SEX TRADE ON THE RELATIONSHIP BETWEEN POLY SUBSTANCE USE AND HIV AMONG SOUTH AFRICANS.

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**Aims:** Coinciding with the HIV/AIDS epidemic in South Africa is increasing rates of illicit drug use. However, few studies have examined moderators of the relationship between substance use and sexually transmitted HIV in southern Africa. Understanding the relationship between sex trade and substance use among South Africans is of considerable importance, given: (1) in sub-Saharan Africa high acquisition and transmission rates among female sex workers and their clients have played a key role in the spread of HIV and for maintaining HIV infection rates; and (2) rising rates of cocaine and heroin. In the present study we examine the extent to which the relationship between substance use and HIV is moderated by involvement in sex trade among a sample of substance users.

**Methods:** Data were drawn from the NEURO STUDY (NIDA-R01-DA14498). Participants included 200 males and 200 females residing in the Pretoria region (mean age 24.4 years). Logistic regression analyses were used to examine the relationship between substance use, sex trade and HIV.

**Results:** For persons involved in sex trade poly substance use was associated with being HIV positive (OR=3.0; 95%CI = 1.04-8.67). No relationship emerged between substance use and HIV among persons not involved in trading sex. However, a relationship emerged between using drugs to cope and HIV status among persons not involved in sex trade (OR=2.6; 95%CI = 1.21-5.66).

**Conclusions:** Substance use may be increasing high risk sexual behaviors of persons involved in exchanging sex for drugs/money and, thereby, resulting in HIV. Also, persons diagnosed with HIV appear to use drugs to cope with its social and health consequences. The rising rates of cocaine and heroin will serve to exacerbate the current HIV epidemic. Therefore, researchers must work with the government and NGOs to prevent substance use and provide treatment for those already involved with drugs, especially high risk groups (e.g., HIV positive individual and persons involved in sex trade).

**Support:** NIDA-R01-DA14498 and NIDA-T32DA007292

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### VALIDATION OF TRIAGE CRITERIA FOR DECIDING WHICH APPARENTLY INEBRIATED PERSONS REQUIRE EMERGENCY DEPARTMENT CARE.

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**Aims:** Some 600,000 emergency department (ED) visits for acute alcohol intoxication occur annually in the US. A half to two-thirds of these appear to be uncomplicated, and might safely be triaged to management in non-ED settings. We hypothesized that expert consensus criteria would provide sensitive and specific triage.

**Methods:** Paramedics collected data on 99 apparently inebriated persons en route to the ED. We retrospectively reviewed these patients' ED charts to assess who required ED care. We then estimated sensitivity and specificity for proposed triage criteria that would have excluded patients from non-ED care: chest or abdominal pain, shortness of breath, suicidal ideation, abnormal vital signs or Glasgow Coma Scale, signs of head trauma, inability to ambulate, seizure, lacerations, fractures, or pregnancy.

**Results:** Subjects were mostly male (89%), homeless (57%), and found on the street (81%); 18 appeared to require ED care, 40 were eligible for non-ED care, but 4 of these would have "bounced back" to the ED (negative predictive value 90%, sensitivity 76%, 95% CI: 50-93%; specificity 44%, 95% CI: 33-55%). Paramedic opinion alone was highly specific (80%) but not very sensitive (41%). Lowering the pulse exclusion threshold from 130 to 83 would increase sensitivity to 100%, but decrease specificity to 22%. A simple post-hoc rule excluding those with age > 55 or pulse > 83 from non-ED care had high sensitivity (94%) and fair specificity (61%). The proposed criteria's sensitivity and specificity varied (65-83% and 44-49%, respectively) depending on which ED services were considered optional (e.g., psychiatric consultation, EKG, IV fluids, etc).

**Conclusions:** Most apparently inebriated individuals do not require ED care, but prospective identification of these persons is a challenge. A low exclusion cutoff for tachycardia may improve sensitivity.

**Support:** DA018179

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### PREDICTORS OF JOB-SEEKING BEHAVIORS.

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**Aims:** The Southwest Node of NIDA's CTN conducted a single-site adaptation of its national Job Seekers Workshop study (Svikis, P.I.) in a Native American treatment program in the American Southwest. Native American participants (N=102) were randomized to either (1) a three session, manualized program (JSW) or (2) a 40-minute Job Interviewing Video (JIV). There was no main effect of treatment. The present secondary analysis tested for potential moderating effects at both the three-month and six-month follow-up points.

**Methods:** Intake data from were assembled from the ASI-Lite, Wide Range Achievement Test, pre-treatment Vocational Survey, and demographics form for study participants. Analyses were conducted to determine whether these variables were predictive of employment status.

**Results:** Participants with higher total reading scores on the WRAT were significantly more likely to be employed at the six-month follow-up ( $\chi^2(1) = 5.577, p < .02$ ). The odds of employment increased for every one-unit increase on the WRAT (OR = 1.06,  $p < .03$ ). The unemployment rate in participants' home region was also a significant predictor of employment at the three-month follow-up ( $\chi^2(5) = 11.773, p < .05$ ). The odds of employment at six months decreased with higher regional unemployment (OR=.576,  $p < .05$ ). Older participants were also more likely to be employed at the six-month follow-up ( $\chi^2(1) = 4.247, p < .04$ ). The odds of employment at six months increased with increasing age (OR = 1.042,  $p < .05$ ). The number of taxed income jobs participants held since their 18th birthdays also predicted employment at six months ( $\chi^2(1) = 6.520, p < .02$ ). The odds of employment increased for each additional job held (OR = 1.091,  $p < .02$ ). Gender and tribal affiliation were not significant predictors of employment at any follow-up.

**Conclusions:** Some variables that predict future employment, such as local unemployment, age, and work history, are not amenable to employment interventions. However, it may be possible to improve employment outcomes by designing interventions to improve reading skill or other job-related skills.

**Support:** NIDA CTN

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# MEASURING THE IMPACT OF CHANGE: DEVELOPING STATEWIDE PROCESS IMPROVEMENT PERFORMANCE MEASUREMENT SYSTEMS.

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**Aims:** This study provides a basis for understanding the fundamental building blocks for developing state-level process improvement performance measurement (PIPM) systems designed to support addiction treatment providers in their efforts to improve access to and retention in treatment.

**Methods:** In fourteen states, the Single State Authorities (SSAs) implemented statewide process improvement learning collaboratives in partnership with addiction treatment providers. The creation of a state-level information system to support process improvement requires a commitment from leadership as well as an investment in the technical infrastructure and human capital to support the critical system components. A primary purpose of a PIPM system is to collect information, measure change, and provide feedback on the impact of process improvement efforts within the state. While most states have not reached this level, the STAR-SI and NIATx 200 initiatives show that some states are beginning to invest financial and human resources into the infrastructure necessary to support a PIPM system. The key lessons learned from this research will be addressed.

**Results:** The results address the role of the state payer and data reporting systems, the need for data collection, data quality, and performance feedback reports, and present a conceptual model for the PIPM framework. We also share lessons learned and strategies for enhancing or developing a PIPM framework at the state level.

**Conclusions:** Performance management is an important component of statewide process improvement collaboratives. These strategies and lessons learned are designed to help states considering the implementation of similar systems.

**Support:** This project was supported by the Center for Substance Abuse Treatment (SC-05-109) and the National Institute on Drug Abuse (5 R01 DA020832-02).

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# PHASE II STUDY OF THE SAFETY AND TOLERABILITY OF NIACIN COMBINED WITH OXYCODONE HCL 5MG VS. OXYCODONE HCL 5MG ALONE IN HEALTHY ADULT SUBJECTS.

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**Aims:** To compare the safety and tolerability of oxycodone HCl 5mg/niacin 30mg or oxycodone HCl 5 mg/niacin 60mg vs. oxycodone HCl 5mg alone. ACUROX<sup>®</sup> Tablets, a unique combination of oxycodone HCl and niacin, are being developed to treat moderate to severe pain, and are designed to produce unpleasant, dysphoric effects when taken in excess of the recommended dose.

**Methods:** Subjects were randomized to 1 of 3 treatment groups (n=22 enrolled to each group). During the Run-in Phase (Days 1-5), subjects received placebo qid (Groups 1 and 2) or niacin 30 mg qid (Group 3). During the Treatment Phase (Days 6-10), subjects received oxycodone HCl 5mg qid (Group 1), oxycodone HCl 5mg/niacin 30mg qid (Group 2) or oxycodone HCl 5mg/niacin 60mg qid (Group 3). Subjects completed a Side Effects and Symptoms Questionnaire (SESQ; scale, 0 to 3) on Days 1-10 and a Tolerability Rating Scale (TRS) before and after the Treatment Phase.

**Results:** At the end of the Run-in Phase, niacin-related side effects and symptoms (eg, flushing, tingling, warm feeling) occurred in 5% of subjects receiving placebo, and 27% of subjects receiving niacin 30mg. In the Treatment Phase, mean SESQ scores in each group were generally low ( $\leq 1.0$  on Day 10) and tended to decrease over time. Most symptoms in the Treatment Phase were niacin-related and mild or moderate in severity. On Day 6, niacin side effects occurred in 9%, 27%, and 32% of subjects in Groups 1, 2, and 3, respectively. On Day 10, niacin side effects occurred in 0%, 9%, and 5% of subjects in Groups 1, 2, and 3, respectively. These data suggest that tolerance to niacin developed. On the TRS, 77% of Groups 2 and 3 rated oxycodone HCl 5mg/niacin as "having no effect" or "easy to tolerate," compared with 73% of Group 1. No serious adverse events occurred.

**Conclusions:** Subjects treated with ACUROX Tablets may experience niacin-induced symptoms that generally decrease within a few days of initiating therapy and have minimal impact on tolerability as measured by a TRS.

**Support:** King Pharmaceuticals<sup>®</sup>, Inc.

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# THE POSTERIOR CINGULATE: A FUNCTIONAL AND STRUCTURAL CORRELATE OF CHRONIC ADMINISTRATION OF THE GABA B AGONIST, BACLOFEN IN SMOKERS.

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**Aims:** The use of the GABA B agonist, baclofen as an anti-relapse agent in alcohol and cocaine dependence is encouraging. Those dependent on cigarettes may also benefit, however this has not been tested. In a smoking reduction trial, baclofen (vs placebo) reduced the number of cigarettes smoked per day. In a subset of smokers that participated in the trial baseline brain data was acquired pre- and following 3 wks medication. Baclofen dampened baseline activity in the anterior cingulate and bilaterally in the ventral striatum, insula and orbitofrontal cortex, and selectively enhanced activity in a circumscribed region of the posterior cingulate. These earlier findings provided evidence of a possible mechanism underlying baclofen's putative utility as a smoking cessation agent. We postulated that the modulation of resting brain activity induced by chronic baclofen may be a function of changes in brain morphology.

**Methods:** We used optimized voxel based morphometry on the same cohort of smokers to examine structural changes that may be a consequence of baclofen administration. Whole brain (unmasked) comparisons of high resolution structural MRIs of pre-medication vs following 3 wks medication were examined (N=10/group).

**Results:** We observed an increase in gray matter density that overlaps considerably with the finding in the functional study (suprathreshold voxel located at -8 -36 31 within a cluster consisting of 1903 contiguous voxels at  $p < 0.001$ , uncorrected). There were no structural differences in placebo subjects.

**Conclusions:** This is the first report that chronic administration of a medication with purported anti-relapse properties, can induce structural changes possessing functional correlates. These data support a growing body of evidence attesting to the possible utility of baclofen as an anti-relapse agent in smokers and other drug-dependent populations.

**Support:** NIH grants DA015149, K01 DA 015426-011A1, 5-P60-DA-005186-18, NS045839, BCS-0224007, RR02305

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# DISSEMINATING EVIDENCE-BASED PRACTICES FOR TREATING CO-OCCURRING DISORDERS IN CHILDREN AND THEIR CAREGIVERS.

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**Aims:** The 2004 California Mental Health Services Act (MHSA) imposed a 1% income tax on personal income in excess of \$1 million, resulting in increased funding to support county mental health programs for consumers of all ages and their families, particularly those with the highest need. In November, 2007, UCLA's Integrated Substance Abuse Programs received a contract from Los Angeles County Department of Mental Health to provide COD training to staff working with Children ages 0-15 and their caregivers.

**Results:** A needs assessment to identify training needs showed that 60% of respondents had worked in mental health fewer than 5 years. COD training interests were greatest in the areas of: providing integrated and trauma-sensitive treatments; addressing COD in caregivers; and developing assessment and engagement skills for COD clients. Training strategies to infuse EBP's into this system included both in-person trainings and on-going focused skill development using onsite Coach/Mentors (licensed mental health professionals) in targeted agencies. Curriculum content emphasized assessment and treatment planning for COD patients, the development of Motivational Interviewing skills for assessment and treatment of COD patients, and strategies for screening and brief intervention. Over 600 staff attended the trainings. Evaluation showed that participants liked the quality and benefits training (more than 85% were highly satisfied). Knowledge increased significantly with improvements of at least 10% from pre to post training.

**Conclusions:** This training program provides an innovative strategy using traditional training and ongoing skill development as a dissemination strategy for developing EBP skills among providers serving a hard-to-treat population.

**Support:** This project was generously funded by Department of Mental Health, Los Angeles, Contract #MH010054

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**CLINICAL GUIDELINES FOR THE MANAGEMENT OF CANNABIS USE DISORDER.**

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**Aims:** To develop evidence based guidelines to support clinical practice in the management of cannabis use disorder. This paper will outline steps that were used to systematically develop clinical guidelines based on evidence supplemented by expert consensus.

**Methods:** The guidelines have been developed from a framework used by Finnish researcher Kettil Bruun. Trigger papers, or literature reviews were prepared by an international panel of cannabis key experts. Discussants researchers with clinical expertise reviewed the trigger papers and made clinical recommendations. Finally a facilitated workshop was attended by key experts and a wider group of clinicians. After reviewing the trigger and discussant papers workshop delegates discussed pivotal points and established consensus on the draft guideline recommendations.

**Results:** Consensus on evidence and clinical practice was achieved and guidelines developed across 8 topic areas

**Conclusions:** A comprehensive set of guideline that outlines background information screening, assessment, brief interventions (including special populations such as families, young people and non-treatment-seekers), withdrawal management and treatment of co-occurring mental health disorders and cannabis use have been developed. These guidelines are suitable for all clinicians who work with cannabis users, regardless of the setting in which they present.

**Support:** Australian Government Department of Health and Ageing

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**SEX DIFFERENCES IN BRAIN RESPONSES TO SMOKING CUES VARY AS A FUNCTION OF SMOKING SATIETY/ABSTINENCE.**

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**Aims:** Exposure to smoking-related cues is a significant trigger precipitating smoking relapse. Smokers find these cues to be highly salient, and the presentation of these cues increase activation of dopaminergic innervated networks in regions subserving attention, goal directed behavior, and reward. However, relatively little is known regarding neurobiological differences between the sexes that may differentially contribute to the maintenance of smoking addiction. The current study sought to evaluate sex differences in the effects of smoking abstinence on smoking cue reactivity.

**Methods:** BOLD-fMRI images were collected in female (n = 12; M cigarettes/day = 18.83, SD = 3.54) and male (n=9; M cigarettes/day = 16.89, SD = 4.01) smokers while viewing blocks of smoking-related and non-smoking matched control cues during two sessions: once following 24 hr abstinence, and once following smoking as usual.

**Results:** Cue-provoked craving did not vary as a function of sex. Smoking cue > Control Cue contrast images were generated. Group (female, male) differences were then analyzed separately for each smoking condition (satiated vs. abstinent) at  $p < .005$ , uncorrected, 10 voxel cluster extent. On the abstinent day, brain activation was greater for females as compared to males in regions involved in drug reward (putamen), attention (anterior & posterior cingulate gyri), processing face stimuli (fusiform gyrus), and primary motor cortex. Male > female activations were not observed for the abstinent condition. On the satiated day, brain activation was greater for males as compared to females in regions involved in drug reward (putamen) and self-awareness (precuneus). Female > male activations were not observed for the satiated condition.

**Conclusions:** These novel results indicate that females and males process smoking-related cues differently as a function of smoking state which may explain, in part, sex differences in cue-provoked craving and cessation outcomes.

**Support:** Research funded by a grant from the National Institute on Drug Abuse (K23DA017261;FJM).

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**INVOLVEMENT OF DOPAMINE SYSTEM ON PSYCHOSTIMULANT-LIKE PROPERTIES OF p-FLUOROAMPHETAMINE IN MICE.**

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**Aims:** The aim of the present study was to investigate the behavioral and neurochemical properties of the amphetamine analogue p-fluoroamphetamine in mice.

**Methods:** In the present behavioral analysis study, we investigated the effect that p-fluoroamphetamine has on the locomotor activity and the place conditioning in ICR mice and whether any of the associated effects discovered might be involved with the dopamine receptors. Furthermore, we focused on both the abilities of p-fluoroamphetamine to inhibit monoamine oxidase (MAO) activities and on the changes in the concentration of dopamine and dopamine metabolites in the mouse limbic forebrain (containing the nucleus accumbens and olfactory tubercle).

**Results:** Administration of p-fluoroamphetamine produced marked hyperlocomotion. In a place conditioning study, p-fluoroamphetamine produced a significant conditioned place preference. The stimulus and rewarding effects of p-fluoroamphetamine were completely suppressed by dopamine D1 receptor antagonist SCH23390. p-Fluoroamphetamine also significantly increased the dopamine content in the limbic forebrain. MAO activities in the limbic forebrain were suppressed by p-fluoroamphetamine.

**Conclusions:** Our findings demonstrated that the dopamine D1 receptors might be involved in the expression of p-fluoroamphetamine-induced hyperlocomotion and the rewarding effect. The monoamine system, which is mainly the dopamine system, may play an important role in the expression of the p-fluoroamphetamine-induced psychostimulant-like effects. Furthermore, the enhancement of the catecholaminergic activity produced by p-fluoroamphetamine may be due to p-fluoroamphetamine's inhibitory effect on MAO activity. These behavioral and neurochemical data indicate that p-fluoroamphetamine might have a psych dependence liability that is similar to psychostimulants.

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**MEDICAID REIMBURSEMENT FOR SCREENING AND BRIEF INTERVENTION OF SUBSTANCE ABUSE.**

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**Aims:** Screening and brief intervention (SBI) can decrease alcohol misuse/abuse and associated burdens to health care systems, including state Medicaid expenditures. In January 2007, the Center for Medicare and Medicaid Services authorized two Healthcare Common Procedural Coding System (HCPCS) Level II codes and individual states may include Medicaid reimbursement for SBI. This study assesses state Medicaid activities toward reimbursing for SBI.

**Methods:** Brief telephone interviews were conducted with 35 states and email information was obtained from 4 states (total n=39; 78% of states). Participants included Medicaid directors, substance abuse state authorities and/or a representative from their state office(s). Interviews included categorical and open-ended questions on reimbursement for SBI.

**Results:** 100% of respondents were familiar with one or more HCPCS Level I or Level II codes for SBI. Twenty-four states have made decisions about proceeding with the codes. Of those, 15 states indicate "yes" they have made a decision on whether or not to implement codes. Six states indicate having "already included the codes in our Medicaid plan." Of those 6 states, 5 are using CPT codes and 1 is using HCPCS Level II codes. Eleven states are "taking action toward implementing" codes, 17 states are "learning about the codes" and 1 state is "choosing not to implement" the codes. 40% of respondents considered implementing the codes a moderate priority and 26% thought full implementation in the next year was somewhat likely. Qualitative themes elucidate key processes, barriers and intentions toward implementing the SBI codes.

**Conclusions:** Findings indicate that very few states have included HCPCS codes for SBI in their state Medicaid plans and that, while many states have intentions to implement or learn more about reimbursement of SBI, the level of activity is limited. Discussion points will focus on implications of the findings for future efforts toward implementing HCPCS codes for SBI.

**Support:** An award from the Robert Wood Johnson Foundation, Substance Abuse Policy Research Program supported this study.

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# REVERSIBLE INACTIVATION OF THE BASOLATERAL AMYGDALA, BUT NOT THE DORSOLATERAL CAUDATE-PUTAMEN, ATTENUATES THE CONSOLIDATION OF COCAINE-CUE ASSOCIATIVE LEARNING IN AN ANIMAL MODEL OF RELAPSE.

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**Aims:** Previous research has shown that the basolateral amygdala (BLA) mediates stimulus-reward learning, including drug-cue associations. In contrast, the dorsolateral caudate putamen (dlCPu) primarily mediates stimulus-response (habit) learning, but the role of the dlCPu in drug-cue learning has received relatively little attention. The current study used a model of pavlovian learning in order to compare the role of the BLA and dlCPu in the consolidation of discrete cocaine-cue associations that affect drug-seeking during reinstatement. We hypothesized that BLA inactivation, but not dlCPu inactivation, would impair associative drug-cue learning and subsequent cocaine-seeking triggered by these conditioned cues.

**Methods:** Male Sprague-Dawley rats (n=15) were trained to self-administer i.v. cocaine (0.2 mg/50 µl infusion) in the absence of cues for 6 days (2 hr sessions). Immediately following a single 1 hr classical conditioning (CC) session in which passive cocaine infusions were paired with a light+tone stimulus, animals received bilateral infusions of the GABA agonists, baclofen and muscimol (B/M, 1.0/0.1 mM), or vehicle into the BLA (0.5 µl/site) or dlCPu (0.6 µl/site). Following additional self-administration (5 days) and subsequent extinction (no cocaine or cues, 7 days), the ability of the previously cocaine-paired cues to reinstate cocaine-seeking was assessed.

**Results:** Post-CC GABA agonist infusions in the BLA impaired conditioned-cue reinstatement as compared to vehicle controls ( $p < 0.05$ ), while similar treatment in the dlCPu was without effect.

**Conclusions:** Overall, these results indicate that while the BLA is involved in the consolidation of stimulus-reward (i.e., cue-cocaine) associations, the previously demonstrated role of the dlCPu in cocaine-seeking during relapse is maintained by stimulus-response learning.

**Support:** (Supported by NIH Grant DA10462)

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# RESPONSE TO NOVELTY PREDICTS BOTH RESPONDING FOR A VISUAL STIMULUS AND SELF-ADMINISTRATION OF A LOW DOSE OF METHAMPHETAMINE IN RATS.

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**Aims:** Self-administration (SA) procedures often pair a visual stimulus (VS) with drug presentation. The psychomotor stimulant nicotine has been shown to enhance the rewarding value of a VS (Donny et al., 2003). It is possible that a VS also acts as a reinforcer in methamphetamine (METH) SA procedures. In this study we determine if response to novelty, which is predictive of SA, is also predictive of responding to produce a VS and examined the role of the VS in SA of low dose METH.

**Methods:** Thirty male Long-Evans rats were placed into novel locomotor chambers and basic activity was recorded. Locomotor scores were used to divide the rats into groups. Animals with high locomotor scores were identified as high responders (HR, n=10, top third of the group) and animals with low locomotor scores were identified as low responders (LR, n=10, bottom third of the group). Subjects in the middle third were not used (n=10). In Phase 1 responses to the active side produced a VS (5 s duration) according to a variable interval (VI) 2 min schedule of reinforcement. Snout pokes to the inactive side had no programmed consequence. Rats were then implanted with chronic indwelling jugular catheters and in Phase 2, snout pokes to the active side produced the VS paired with an intravenous infusion of 0.025 mg/kg METH according to a VI 2 min schedule of reinforcement.

**Results:** In phase 1, rats classified as HRs responded significantly more for the VS than rats classified as LR indicating that response to novelty and reinforcement by a VS are related. In Phase 2, HRs, but not LR, increased responding to the side on which the VS was paired with drug, indicating that the VS/METH combination acted as a reinforcer only for the HR group.

**Conclusions:** These results indicate that response to novelty and the reinforcing properties of the VS reflect similar neural/behavioral processes and that light reinforcement may influence acquisition of low dose METH SA.

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**Support:** DA21261

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# DEXTROAMPHETAMINE AS A TREATMENT FOR METHAMPHETAMINE DEPENDENCE.

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**Aims:** Substitution treatment is effective in nicotine and opiate dependence but efficacy in methamphetamine dependence has not been established. We conducted a trial to assess the safety and efficacy of dextroamphetamine as a substitution treatment for methamphetamine dependence.

**Methods:** Methamphetamine dependent outpatients were randomized to 30 mg sustained release oral dextroamphetamine twice per day (N=16) or matched placebo (N=14). Adverse events and urine toxicology for methamphetamine were assessed twice per week for 8 weeks. Urine samples with  $< 1,000$  ng/mL of methamphetamine were classified as negative. A preplanned interim analysis was conducted.

**Results:** There were no serious adverse events. The proportions of subjects reporting other adverse events did not differ by group. There was a trend ( $p=0.19$ ) toward more methamphetamine negative urine samples in the dextroamphetamine group ( $3.1 \pm \text{sd } 4.7$ ) than in the placebo group ( $1.4 \pm \text{sd } 2.3$ ). **Conclusions:** Dextroamphetamine 30 mg twice per day does not appear to be less safe than placebo in methamphetamine users. Its safety and the trend toward greater efficacy in the dextroamphetamine group warrant continued enrollment of the planned sample of 60 subjects.

**Support:** DA018179

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# GENDER DIFFERENCES IN TOBACCO USE AND SMOKING RISK FACTORS AMONG SPANISH ADOLESCENTS.

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**Aims:** Smoking among adolescents is one of the main concerns for the Public health care system in Spain. The number of boys who start smoking is relatively stable with a downward trend since decades ago, quite the opposite of girls. The number of smoking girls is growing faster and gender differences are reducing. This fact is in harmony with Stage III proposed by Lopez et al. with regard to evolution of tobacco use in developed countries. The objectives of the present study are to analyze gender differences in tobacco use among adolescents, as well to determine gender differences in risk factors to use cigarettes.

**Methods:** The study sample of 1483 boys and 1358 girls, aged 12-16 (M=14), was extracted from 10 High Schools from Barcelona, Spain. Participants were asked to answer an ad-hoc instrument to evaluate pattern of use and traditional risk factors to smoke tobacco (perceived availability, risk of harm, family- and peer- use and engage in leisure activities). They were also asked to fill two other scales to assess drive for thinness (DT from EDI-2) and The Rosenberg self-esteem scale. Chi-square and Student t test analysis was used to determine gender differences in pattern of use and risk factors.

**Results:** We didn't find gender differences in the pattern of use except for age of first use. With regard to risk factors we did find gender differences in some of the variables assessed: risk perception, engage in leisure activities, self-esteem and drive for thinness but we didn't find differences in the rest of variables: perceived availability and family- or peer- use.

**Conclusions:** Results indicate some gender differences, not in the frequency or pattern of use as hypothesized but in some of the risk factors traditionally associated with drugs and tobacco use. The findings help increase our understanding of gender differences related with smoking risk factors and to pay special attention to the specific needs of girls and boys when planning prevention programs to reduce risk factors.

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### THE EFFECTS OF WEIGHT LOSS AND METHAMPHETAMINE ADMINISTRATION ON HORMONE LEVELS.

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**Aims:** The effects of methamphetamine (Meth) include distinct behavioral and physical changes. These effects may, in part, be a secondary symptom resulting from altered hormone levels. The rapid weight loss experienced by Meth abusers may result in changes in hormone levels. We theorize that the Meth-induced rapid metabolism of fat stores (releasing sequestered gonadal hormones) may be capable of a substantial increase in the concentration of these hormones into the bloodstream that could result in a myriad of behavioral effects. Our aim in this study was to document the potential fluctuations in hormone levels, specifically corticosterone and testosterone as a function of weight loss induced by Meth administration.

**Methods:** Twenty-four adult male Wistar rats weighing 650-750 g were randomly separated into free-fed and caloric-restricted groups. Each of these groups was then further subdivided into groups receiving intraperitoneal injections of saline or Meth. The Meth treatment groups received a 5-day escalating dose regimen of Meth injections beginning with 0.5 mg/kg and ending at 4.0 mg/kg (in order to build tolerance to the lethal effects of Meth). The groups received Meth or saline according to a binge schedule of administration modified from Kuczenski and Segal, 1999. One mL of blood was collected daily from each animal via an indwelling catheter and plasma isolated from these samples was frozen at -20°C for later analysis using Elisa kits for corticosterone and testosterone.

**Results:** Our results showed a significant decrease in plasma testosterone and an initial increase of plasma corticosterone in the Meth-treated groups.

**Conclusions:** The decrease in testosterone may be related to the sexual dysfunction often reported with Meth abuse in humans. This, together with increased levels of corticosterone (indicating an initial activation of the HPA axis) may contribute to the violent behavior sometimes observed in chronic Meth abusers.

**Support:** USPHS Grant DA06013 from the National Institute on Drug Abuse

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### DISAGGREGATING A NEIGHBORHOOD PERCEPTION SCALE BY HEROIN DEPENDENCE.

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**Aims:** The association between social disorder and substance abuse has been documented, though literature on neighborhood perceptions and heroin dependence is sparse.

**Methods:** A community-based sample of 1034 non (NDU), former (FNU), non-injection (NIDU) and injection drug users (IDU) aged ≥18 years were recruited in New York City. Bivariate analyses assessed the relationship between heroin dependence and self-reported neighborhood perceptions of neighborhood violence, neighborhood problems, and safety from crime (Echeverria, et al., J Urban Health, 2004).

**Results:** Our sample was 69% male, 48% black and 42% Hispanic; mean age was 40 years. Heroin dependent subjects perceived more neighborhood problems and felt their neighborhoods were less safe than non-dependent subjects; differences were minimal. Multivariate logistic regression models showed no significant relationship between neighborhood perceptions and heroin dependence after adjusting for demographics. We disaggregated the measures in order to assess their performance. We compared our means, standard deviations, and Cronbach's alphas for the three subscales to those of Echeverria, et al.; all were similar. We observed an increasing trend for perceptions of violence such that NDU perceived the least violence and FNU the most. Though statistically significant, qualitatively there was little difference between subgroups. We then disaggregated the measures, comparing the means of each scale/item among heroin dependent vs non-dependent. There were significant differences for most items in the neighborhood problems index and one item on the safety from crime scale, qualitatively the differences were small.

**Conclusions:** Our analysis suggests that these measures may not adequately capture differences in neighborhood perceptions among drug-using subgroups; a wider response scale may be necessary. Researchers should further examine scale and index items before administering to complex subgroups.

**Support:** This study was partly funded by grants DA018061, DA017020, and MH068192 from the National Institute on Drug Abuse and the National Institute of Mental Health.

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### BOTH IMAGERY SCRIPTS AND MENTAL ARITHMETIC INDUCE STRESS IN METHAMPHETAMINE USERS.

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**Aims:** Patients treated for methamphetamine (MA) dependence have a high rate of relapse and stress is thought to play a key role. Stress reactivity may therefore be an important determinant of relapse. Personalized stress imagery scripts are effective in cocaine users but are time consuming to implement. We sought to develop a computerized procedure for inducing stress in MA users.

**Methods:** In a within-subjects design, we compared the effects of personalized stress imagery scripts to a novel difficult mental arithmetic task with financial incentives and a control condition (neutral imagery) in 10 former MA users. Self-report responses were assessed with two 100 mm visual analog (VA) items (anxiety and craving) and the Positive and Negative Affect Schedule (PANAS). Responses were assessed immediately prior to each condition and 0, 15, and 30 minutes after each condition. We hypothesized that both procedures would be effective in inducing stress in MA users.

**Results:** There were main effects of condition and time for VA anxiety (condition:  $F(2,98)=3.9$ ,  $p=0.02$ ; time:  $F(3,98)=11.3$ ,  $p<0.0001$ ) and PANAS negative affect scores (condition:  $F(2,98)=4.8$ ,  $p=0.01$ ; time:  $F(3,98)=11.1$ ,  $p<0.0001$ ). Compared to the control condition, both the math task and stress scripts increased VA anxiety immediately after the intervention ( $p<0.001$ ,  $p=0.022$ , respectively) and increased PANAS negative affect (both  $p<0.0001$ ). VA anxiety change scores were 12.5, 10.5, and -4.4 for the math, stress, and control conditions, respectively. PANAS negative affect change scores were 0.50, 0.40, -0.07 for the same three conditions. Positive affect and craving were not significantly affected.

**Conclusions:** Both the math task and the stress script paradigm were effective in inducing stress in MA users. Because the math task requires less time of staff and participants, it may be a useful alternative for measuring stress reactivity in drug users.

**Support:** DA018179

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### DISCRIMINATIVE STIMULUS EFFECTS OF THE HALLUCINOGEN 5-METHOXY-N-ISOPROPYL-N-METHYLTRYPTAMINE.

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**Aims:** 5-Methoxy-N-isopropyl-N-methyltryptamine (5-MeO-MIPT) is a recreationally used hallucinogenic compound structurally related to other tryptamine hallucinogens. Behavioral and pharmacological effects of 5-MeO-MIPT have not been characterized in laboratory studies.

**Methods:** The effects of 5-MeO-MIPT on locomotor activity was tested in mice. 5-MeO-MIPT was tested in rats trained to discriminate hallucinogenic and psychostimulant compounds, including cocaine, methamphetamine, 3,4-methylenedioxymethylamphetamine (MDMA), lysergic acid diethylamine (LSD), (-)-2,5-dimethoxy-4-methylamphetamine (DOM), and dimethyltryptamine (DMT).

**Results:** 5-MeO-MIPT produced both stimulation and depression of locomotor activity. Depressant effects occurred within 10 minutes following 30 mg/kg and lasted 30 to 80 minutes. Stimulant effects occurred within 50 minutes following 10 mg/kg and lasted 110 minutes. Because of these two different effects on locomotor activity, 5-MeO-MIPT was tested at 15 and 60 minutes in the drug discrimination task. 5-MeO-MIPT fully substituted for DOM ( $ED_{50}=0.61$  mg/kg) when tested 60 min after administration. 5-MeO-MIPT partially substituted for LSD, DMT, and MDMA at both time points, and for DOM at 15 min after administration. 5-MeO-MIPT failed to substitute for cocaine and methamphetamine. Substantial rate suppression was observed at 15 min following 2.5 and 5 mg/kg 5-MeO-MIPT. Higher doses were necessary to produce substantial rate depression at 60 min. These doses produced adverse effects, including tremors and rear leg paralysis.

**Conclusions:** Because 5-MeO-MIPT mostly produced only modest hallucinogenic effects and no psychostimulant effects, but produced substantial adverse effects, it may have limited abuse liability. However, because human users report that it is a very long-acting compound, testing at longer pretreatment times may be necessary to find peak effects. Alternatively, 5-MeO-MIPT may be qualitatively different from other hallucinogens.

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# AN INVESTIGATION OF THE GENDER SPECIFIC RELATIONSHIP BETWEEN CHILDHOOD TRAUMA AND LOW DISTRESS TOLERANCE AMONG LOW INCOME MINORITY SUBSTANCE USERS.

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**Aims:** It is estimated that 25% of substance using women have experienced some form of childhood trauma (CT), and this is especially relevant to low income minority women. Evidence indicates high rates of emotion regulation difficulties among individuals with a history of CT, is also associated with poor substance use outcomes. Of particular interest is the role of distress tolerance (DT), defined as the ability to persist in goal directed behavior when experiencing emotional distress. DT, is a well established predictor of poor substance use outcomes, yet has not been studied in its relationship to CT. As such, the current study aimed to examine the relationship between CT and DT among a mixed-gender sample of substance users, to provide preliminary data of potential mechanisms underlying the relationship between childhood trauma and substance users.

**Methods:** 190 low income, predominately African-American, residents of an inner-city residential drug treatment center completed the Childhood Trauma Questionnaire-Short Form to assess history of physical, sexual, and emotional abuse, as well as completed a computerized behavioral measure of DT (Mirror Tracing Persistence Task). Psychiatric diagnoses were assessed with the Structured Clinical Interview for DSM-IV(SCID-IV).

**Results:** Among women, univariate analyses revealed a significant relationship between low distress tolerance and higher rates of childhood sexual abuse, but not physical or emotional abuse. There was no relationship between distress tolerance and childhood trauma among men. Controlling for BPD, logistic regression analysis indicated that sexual abuse was a unique predictor of low distress tolerance among women ( $X^2=8.09$ ,  $p=.013$ ).

**Conclusions:** These findings demonstrate a link between childhood sexual abuse and distress tolerance among female illicit substance users. They also provide preliminary data for understanding potential mechanisms underlying the relationship between childhood sexual abuse and adult substance use outcomes, and calls for further research.

**Support:** NIDA R01DA19405;R21DA022741

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# DIFFERENTIAL ATTENUATION OF THE DISCRIMINATIVE STIMULUS EFFECTS OF BENZODIAZEPINES AND NEUROACTIVE STEROIDS BY FLUMAZENIL OR PENTYLENETETRAZOLE IN DIAZEPAM-TREATED RHESUS MONKEYS.

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**Aims:** Despite their similar behavioral effects, the potency of positive GABA<sub>A</sub> receptor modulators acting at benzodiazepine or neuroactive steroid sites is differentially modified by chronic diazepam treatment. Changes in GABA<sub>A</sub> receptors that account for these differences are not known. One behavioral approach that can begin to elucidate these changes is to determine whether chronic treatment alters the nature of interactions between drugs acting at the same or different sites.

**Methods:** Two groups of four monkeys were used: one group received 5.6 mg/kg of diazepam daily and discriminated 0.1 mg/kg of flumazenil, a neutral modulator acting at benzodiazepine sites, and the other untreated group discriminated 0.178 mg/kg of the benzodiazepine midazolam.

**Results:** The training dose of flumazenil or 32 mg/kg of pentylenetetrazole (a negative modulator that does not act at benzodiazepine or neuroactive steroid sites) produced >80% flumazenil-lever responding and the effects of each were reversed by positive modulators acting at benzodiazepine or neuroactive steroid sites (midazolam and pregnanolone, respectively). When a larger dose of flumazenil was administered, a larger dose of midazolam was needed to reverse flumazenil-lever responding; however, increasing the dose of flumazenil did not change the dose of pregnanolone needed to produce the same effect. When a larger dose of pentylenetetrazole was administered, larger doses of both positive modulators were needed to reverse flumazenil-lever responding. In untreated monkeys discriminating midazolam, flumazenil antagonized the effects of midazolam and not those of pregnanolone while pentylenetetrazole antagonized the effects of both positive modulators.

**Conclusions:** Thus, chronic diazepam treatment does not alter the qualitative nature of interactions between positive and negative GABA<sub>A</sub> receptor modulators acting at the same or different sites, suggesting that the sites are not fundamentally changed by this treatment.

**Support:** Supported by USPHS grant DA09157 and DA17918 (CPF).

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# A NEW BROAD-SPECTRUM ANTI-METHAMPHETAMINE MONOCLONAL ANTIBODY REVERSES ACUTE METH EFFECTS IN RATS.

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**Aims:** With targeted hapten design, the specificity of anti-drug mAb may be optimized. These studies determined whether anti-METH mAb specificity for METH is important in reversing the effects of an acute dose of METH.

**Methods:** Two new anti-METH mAb were tested, one with specificity for METH (mAb7F9; KD(METH)=1.8nM), and one with specificity for METH and amphetamine (mAb4G9; KD(METH)= 34nM, KD(amphetamine)=120nM). Rats (n=6/mAb dose; 48 total) received METH (1 mg/kg, iv) followed 30 min later by one of four mAb doses (or placebo) which ranged from 0.1 to 1 mol-eq (36.2-362 mg/kg) to the METH dose. Horizontal locomotion and rearing events were measured. A two-way RM ANOVA with dose and treatment (placebo & mAb) as the main factors was used to determine activity differences with placebo compared to antibody. For all pairwise comparisons, Tukey's test was used.

**Results:** Both mAb reduced METH effects by 4 min after mAb dosing. Compared to saline, mAb4G9 reduced the highest value for horizontal locomotion by 26 & 33%, and rearing events by 13 & 37% at the 0.56 and 1 mol-eq doses, respectively. mAb7F9 decreased the highest value for rearing events by 16 & 35% at these two mAb doses, respectively. mAb4G9 reduced the total distance traveled by 32, 47, and 62%, at the 0.32, 0.56, and 1 mol-eq doses, respectively. It reduced the total rearing events by 40, 42, and 66%, at these three mAb doses, respectively. mAb7F9 reduced total distance by 36, 36, and 63%, at these three mAb doses, respectively. Similar results were observed for rearing, and for the duration of increased activity for both mAb. All reported results were significant ( $p<0.05$ ).

**Conclusions:** A high affinity, broad-spectrum anti-METH mAb reduced spontaneous locomotor activity as effectively as a mono-specific mAb. Furthermore, the effective mAb doses were lower than previously reported.

**Support:** R01DA11560; P01DA14361

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# DES-FORMYLFLUSTRABROMINE AND ITS ANALOGS AS POSITIVE ALLOSTERIC MODULATORS OF $\alpha 4\beta 2$ NEURONAL NICOTINIC RECEPTORS.

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**Aims:** Nicotinic acetylcholine receptors (nAChR) have been associated with memory, cognition, and attention processes, and have been shown to play a role in several neurological disorders, providing new valuable targets in the treatment of such conditions. Activation of nAChRs through orthosteric sites would most likely result in receptor desensitization, reducing efficacy of treatment. Recently, several classes of molecules were shown to act as nonselective allosteric modulators of nAChRs. Our group previously reported the synthesis of des-formylflustrabromine (dFBr) and revealed its selective potentiating activity at  $\alpha 4\beta 2$  nAChRs. The present investigation was designed to determine structural features important for the actions of dFBr.

**Methods:** Critical structural features for  $\alpha 4\beta 2$  nAChR potentiation were identified by employing the deconstruction-reconstruction-elaboration method. Proposed compounds were prepared using several synthetic schemes. Biological activities of synthesized compounds were evaluated using two-electrode voltage clamp techniques employing *Xenopus laevis* oocytes injected with cDNAs of the human  $\alpha 4\beta 2$  receptor.

**Results:** A comparison of the ability of the new analogs with that of dFBr to potentiate the actions of acetylcholine revealed the importance, or lack thereof, of key structural features. At least one of the novel compounds was equipotent with dFBr.

**Conclusions:** Allosteric modulators of nACh receptors can be used as probes for understanding possible mechanism underlying the pharmacology of nAChR. Such molecules would have certain advantages over current methods of receptor activation. Here, dFBr and its synthetic analogs were shown to be positive allosteric modulators of  $\alpha 4\beta 2$  nAChRs and key structural features have been identified for this action.

**Support:** Supported, in part, by a Virginia Center on Aging grant and a VCU Department of Pharmacology Training Grant.

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**MODAFINIL IMPROVES COGNITIVE PERFORMANCE IN METHAMPHETAMINE ABUSERS: EVIDENCE FROM HUMAN BEHAVIORAL AND FMRI STUDIES.**

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**Aims:** We performed a double-blind, placebo-controlled study to determine behavioral and neural effects of modafinil on cognitive performance in MA-dependent (N=12) and matched healthy control participants (N=16).

**Methods:** Each participant performed a reversal learning task (RLT) during fMRI scanning on two separate days - one with modafinil administration and another with placebo. The RLT testing the ability to inhibit a prepotent, learned response in favor of a more advantageous alternative response after reward contingencies have changed. The task taxes both cognitive control and working memory.

**Results:** Modafinil raised learning accuracy in the MA group to levels of the control group (from 70% to 96% correct), whereas the control group showed no effect of drug. During reversal trials, requiring the greatest effort in inhibiting a previously learned correct response, the MA group showed worse performance than the control group (60-70% vs. 75-90% correct) with a slight improvement in performance on medication. We found greater recruitment of bilateral VLPFC, hippocampus, and supplementary motor area (SMA)/anterior cingulate cortex (ACC) for modafinil versus placebo in the MA group, but no differences in these regions were found across medication conditions in the control group. This suggests that the medication boosted responses in these regions, sharpening and stabilizing cognitive performance. Moreover, brain activation in these regions correlated with behavioral performance across groups and medication conditions, further showing the importance of these regions for task performance.

**Conclusions:** Results indicate that, in MA-dependent subjects, modafinil boosts cognitive performance and increases brain activation in regions that support essential cognitive functions, such as focused attention and working memory, which are critical for successful outcomes in behavioral treatments (e.g., cognitive-behavioral therapy).

**Support:** DA020726, RR00865, DA022539, DA024853

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**THE EFFECT OF LONG AND SHORT ACCESS TO D-AMPHETAMINE SELF-ADMINISTRATION ON A DELAY DISCOUNTING TASK IN RATS.**

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**Aims:** Impulsive choice, or preference for immediate over delayed gratification, has been indicated in stimulant abuse. D-amphetamine is a widely prescribed ADHD medication, but little is known about its effects on impulsive choice when use becomes dysregulated. We examined the effects of long and short access to d-amphetamine on a delay discounting task, in which rats chose between a smaller sooner reward (one sucrose pellet immediately) and a larger later reward (three sucrose pellets after an adjusting delay).

**Methods:** Preference for the immediate smaller reward was considered more impulsive, whereas preference for the larger, delayed reward was considered more self-controlled. Following choice stability in delay discounting, all rats received 15 1-hr sessions of d-amphetamine self-administration (0.1 or 0.03 mg/kg/infusion); self-administration sessions begin 45 min after each delay discounting session. Rats were then either maintained on the short access (ShA) self-administration session or were switched to a long access (LgA) 6-hr session for 21 days.

**Results:** Rats in the LgA groups at both unit doses showed decreased mean adjusted delays (sec) during the 21-day escalation period compared to the ShA groups, indicating that long access to d-amphetamine increases impulsive choice. Following completion of the 21 day escalation period, all rats received a 7 day withdrawal period. LgA groups returned back to baseline mean adjusted delays, indicating the effect on impulsivity was reversible.

**Conclusions:** These results show that extended use of d-amphetamine produces a transient loss of inhibitory control, which may play a role in the dysregulated escalating pattern of drug intake that characterizes the process of addiction.

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**DECREASES IN DOPAMINE D2 RECEPTOR AVAILABILITY ARE ASSOCIATED WITH AGE IN JUVENILE RHESUS MONKEYS.**

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**Aims:** Dysfunction of the dopamine system has been shown to be associated with a multitude of neuropsychiatric disorders including schizophrenia, attention-deficit hyperactivity disorder, and drug addiction. Adolescence is a time of increased vulnerability to these disorders. It is, therefore, important to understand the normal development of the dopamine (DA) system during the critical period of growth leading up to adolescence.

**Methods:** Sixteen juvenile male rhesus monkeys were scanned with positron emission tomography and the DA D2 receptor ligand, [18F]fluoroclozapine (FCP). Four monkeys were rescanned after 12 months. Data were analyzed using PMOD software (PMOD Technologies, Switzerland) and distribution volume ratios (DVR) were calculated for binding in the caudate nucleus and putamen. The correlation between age at time of scan and D2 DVR was examined.

**Results:** There was a significant negative correlation between age and [18F]FCP DVRs in both the caudate nucleus ( $r = -0.44$ ,  $p < .05$ ) and putamen ( $r = -0.52$ ,  $p < .02$ ). In addition, monkeys that were re-scanned at 12 months showed an average 14.4% decrease in the availability of D2 receptors in the putamen ( $p < .05$ ) and a 14.3% decrease in the caudate nucleus.

**Conclusions:** The development of the DA system in juvenile rhesus monkeys includes a decrease over time of D2 receptor availability in the putamen and caudate nucleus. This decrease could indicate a reduction in D2 receptor number or an increase in synaptic DA levels. It also may reflect a lower D2 receptor density associated with the rapid growth of brain volume during this period. Low levels of D2 receptor availability are associated with increased self-administration of drugs such as alcohol and cocaine. It is therefore possible that normal decreases in D2 receptor density in adolescents may make this age group more susceptible to risk-taking and drug experimentation.

**Support:** DA20648 and DA06634

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**EFFECTS OF PSYCHOSOCIAL TREATMENT DOSE ON OUTCOMES IN STIMULANT-DEPENDENT ADULTS.**

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**Aims:** Presently, there is little empirical evidence from controlled studies to inform clinical recommendations regarding the optimal "dose" of psychosocial addiction treatment. To address this, two studies of stimulant-dependent adults entering treatment examined the relationship between treatment "dose," client compliance and outcomes.

**Methods:** To evaluate the effects of treatment duration on outcomes, in Study 1, 85 participants were randomly assigned to receive either 4 or 16 weeks of outpatient treatment delivered three times weekly. To evaluate the effects of treatment frequency on outcomes, Study 2 included 86 adults who were randomly assigned to receive treatment either once or three times weekly over 12 weeks. Participants in both studies were reassessed using urine tests for stimulant use at discharge, 6, and 12 months post-treatment. The treatment content was identical for each of the conditions across studies, comprising content from the Matrix Model.

**Results:** In Study 1, those in the 16-week condition evidenced greater rates of stimulant-free urines overall ( $\chi^2(1)=7.4$ ,  $p<0.01$ ), relative to those in the 4-week condition (OR=3.3, 95% CI=1.4-7.8). However, in both studies, reductions in stimulant use across time were significant and comparable between the treatment groups. Nevertheless, client compliance, as measured by both the number and percentage of prescribed sessions attended was significantly associated with stimulant use both during and after treatment regardless of the prescribed treatment dose. Those who completed treatment in Study 1 had odds of negative urines 5.5 times those of non-completers (95% C.I.=2.2-13.0); likewise, in Study 2, the odds of negative urines among completers were 2.2 times those of non-completers (95% C.I.=1.1-4.5).

**Conclusions:** Among stimulant-dependent adults randomly assigned to receive psychosocial treatment of varying duration and frequency, the most salient predictor of stimulant use outcomes is compliance with the prescribed treatment regimen.

**Support:** The research presented herein was supported by National Institute on Drug Abuse grants 1K23DA020085 and 1R01DA11972-01.

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### PRELIMINARY FINDINGS FROM A RANDOMIZED CLINICAL TRIAL EXAMINING ASSERTIVE CONTINUING CARE WITH TWO TYPES OF OUTPATIENT TREATMENT FOR ADOLESCENTS.

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**Aims:** The relative effectiveness of two types of outpatient treatment with and without continuing care and their interaction during the 9 months following adolescents' admission to outpatient treatment were examined.

**Methods:** The study design was a randomized 2 (type of outpatient treatment) X 2 (type of continuing care) factorial design, with repeated measures (intake, 3-, 6-, and 9-months). The two types of outpatient treatment were a 5-session Motivational Enhancement Therapy/Cognitive Therapy model plus 2 family sessions (MET/CBT7), and Chestnut's Bloomington Outpatient (CBOP) model, which included group therapy, group skills training, individual, and family sessions. The two continuing care conditions were Assertive Continuing Care (ACC) or no continuing care. Adolescents admitted to outpatient treatment for substance abuse were recruited for the study. Based on 311 adolescents who agreed to participate in the study and provided data for all time points, the average age was 15.8 years old, 76% were male, 74% were Caucasian, and 12% were African American. Seventy percent met criteria for past year cannabis abuse or dependence, while 43% met criteria for past year alcohol abuse or dependence. **Results:** There was a significant time effect for percent of days abstinent in the community  $F(3, 764) = 7.07, p < .001$ , primarily due to the increase in the number of days abstinent between intake ( $M = 71\%$ ) and 3-month follow-up ( $M = 84\%$ ). There was also a significant time by group interaction  $F(8, 764) = 2.24, p < .05$ . Post-hoc simple effects tests revealed a significant linear trend for the CBOP/ACC condition with abstinence increasing over time. For the MET/CBT7 conditions (regardless of continuing care condition), there was a significant non-linear trend for an increased percent of days abstinent from intake to 3 months, which was not maintained at 6 and 9 months. There were no significant findings for the CBOP/UCC condition.

**Conclusions:** The most effective and sustained outcomes were for adolescents who participated in the CBOP plus ACC condition.

**Support:** NIDA DA 018183

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### SECONDHAND EXPOSURE TO SMOKED OPIUM.

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**Aims:** According to the United Nations, there are a million opium addicts in Afghanistan and over half of these are under the age of 15. The effects of opium use are well understood however, the effects of secondhand smoke exposure have yet to be addressed. This study aims to better understand the environment of opium smokers and those living in the immediate vicinity.

**Methods:** Methods previously applied to testing for secondhand cigarette smoke and drug residues on surfaces were used to ascertain the presence and levels of opium-related drugs in households of Kabul, Kandahar and Badakhshan Province, Afghanistan. Seven homes of recovering opium addicts and three control homes were tested. All inhabitants of the homes provided consent. Five areas in each home (e.g., walls, floors, tables) were swabbed for surface contamination and hair was obtained from each inhabitant. The swabs were tested for opiates using a specially designed lateral flow drug test strip and elution fluid. Surface testing was confirmed by LC-MS/MS by U.S. Drug Testing Laboratories.

**Results:** Of 10 homes, 7 were positive for opium on surfaces and 5 of the homes had inhabitants testing positive for opium by hair analysis. Of 12 opium-positive inhabitants, 8 were children, with ages ranging from 14 months to 12 years. Four of the hair samples revealed the presence of 6-acetylmorphine, which indicates the presence of not only opium, but heroin exposure. Additionally, three homes were tested for the presence of opium-related drugs in the air and two tested positive.

**Conclusions:** Many of these children are unwilling victims of this public health tragedy. Smoking opium can produce secondhand vapors and residues that can be readily inhaled or absorbed through the skin and should not be in a child's environment. Future research will focus on determining the extent of exposure to surfaces contaminated with opium residues vs. inhalation.

**Support:** Supported by the U.S. Department of State International Narcotics and Law Enforcement Affairs.

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### METHAMPHETAMINE USE: DOES IT INCREASE VIOLENT SEXUAL ACTIVITY IN WOMEN?

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**Aims:** Although there are scant instances in the scientific literature, a perusal of newspaper and online news reports highlights a significant association among methamphetamine (meth) use, violence, and risky/unusual sexual practices. This violent sexual activity is thought to be predominantly male-perpetrated, but numerous accounts suggest that women who are heavy users of meth are also engaging in violence and unusual sexual activity.

**Results:** Instances of sexual and other abuses perpetrated by men are widespread and well-known. Such activities are much less commonly committed by women. Although many women initially start using meth to lose weight, most continue to use it because of its highly addictive properties. Surprisingly, while the male-to-female ratios for cocaine users are 2:1 and 3:1 for heroin, the ratio for meth is an astounding 1:1, a ratio not seen with any other drug except possibly alcohol. Clearly, women are at a greater risk for meth dependence than for any other drug. Furthermore, although initial use of meth can enhance sexual encounters, chronic use of this drug may contribute to a need for increasingly risky and/or unusual sexual behaviors in both men and women, in order to maintain sexual arousal, enhance satisfaction, or generally to maintain a sense of intimacy. These unusual sexual behaviors may extend beyond the confines of an intimate relationship and may involve violence, which itself seems to be exacerbated by the use of meth in both men and women. The end result of this trajectory could be violent sexual crimes, which seem to be on the uprise, particularly in areas severely affected by the meth epidemic.

**Conclusions:** Conclusion: Although it is not clear whether methamphetamine is a causal factor for increased violence and unusual sexual activity in women or is mainly disinhibiting underlying tendencies, this is clearly an area that deserves further attention due to the implications both for women's health and public health/safety.

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### DRONABINOL BLUNTS DRUG CUE REACTIVITY IN MARIJUANA-DEPENDENT PATIENTS.

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**Aims:** Prior research in our laboratory has demonstrated that drug cues (for cocaine, nicotine and opiates) activate limbic reward circuitry. We hypothesized that cues for marijuana would similarly activate limbic reward regions (e.g., amygdala, ventral striatum, ventromedial prefrontal cortex, insula) in treatment-seeking marijuana patients. Further, we wanted to test the effect of dronabinol (synthetic THC), an agonist treatment, on the brain responses to marijuana drug cues in these same individuals.

**Methods:** Subjects (N=11) underwent BOLD fMRI scans during a block design featuring marijuana and non-drug cue task (6 repetitions of MJ and Neutral blocks in a Gellerman series, each cue block presenting 10 still-frame 1.5 sec images) at baseline, and again on medication (dronabinol, N=7; placebo, N=4; ongoing) in a randomized, placebo-controlled study. All subjects had at least a 10- year history of marijuana dependence and smoked at least 2 joints/day on at least 5 days/week.

**Results:** SPM2 contrasts (cluster corrected  $p < .001$ ;  $2 < t < 5$ ) conducted on "drug" minus "neutral" cues demonstrated significantly greater amygdalar and VMPFC activation to marijuana cues when compared to neutral cues at baseline for both groups (placebo and dronabinol). Paired t-tests demonstrated a reduction in limbic (amygdala, VMPFC, parahippocampus, and anterior insula) activation to marijuana vs. non-drug cues in the dronabinol group; no such reduction was observed in the placebo group.

**Conclusions:** Our data show that marijuana dependent subjects have clear limbic activation to marijuana cues, underscoring the shared brain circuitry for anticipation of drug (cocaine, nicotine, opiate, marijuana) reward. This pilot study also provides initial evidence that the cannabinoid agonist dronabinol blunts limbic reactivity to marijuana cues, highlighting the potential of this agent for treatment in marijuana dependence.

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**TREATMENT IMPACT ON HEALTH RELATED QUALITY OF LIFE AMONG METHAMPHETAMINE-DEPENDENT INDIVIDUALS.**

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**Aims:** This study applies a chronic illness framework to the evaluation of substance abuse treatment for methamphetamine (MA)-dependent individuals.

**Methods:** Using growth curve modeling, health-related quality of life (HRQOL) trajectories of methamphetamine (MA) dependent individuals (N=723) were examined over a 12-month period.

**Results:** Results: We found differential improvements in HRQOL, with substantial improvements in mental health status as a function of treatment completion and continued treatment and fairly static trajectories in physical health status. Differences in HRQOL trajectories were observed by gender, psychosocial functioning, drug severity, and health impairment.

**Conclusions:** Results extend research on treatment outcome evaluations for MA dependence and provide useful insight into the course of recovery for MA-dependent users in relation to HRQOL outcomes.

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**MU-OPIOID RECEPTORS ON RED BLOOD CELLS OF COCAINE USERS.**

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**Aims:** Animal studies and human PET studies (Gorelick et al., 2008) show that cocaine use increases regional brain mu-opioid receptor (mOR) binding. This study evaluated whether cocaine use influences the proportion of peripheral red blood cells (RBCs) with mORs (mOR level).

**Methods:** RBCs were collected from peripheral venous blood obtained from 14 cocaine users (8 African-American men, 3 African-American women, 3 white men, mean [SD] age 38.5 [4.9] years, 12.6 [7.2] years of cocaine use, 19.1 [7.8] days of cocaine use in month prior to study screening) with current abuse/dependence, but little use of other illegal drugs or alcohol. Ten were current cigarette smokers. mOR level was measured by flow cytometry with an anti-mOR antibody. Eleven subjects also had 2-5 measurements over 24.1 [18.5] weeks (range 2.3-52.3 weeks).

**Results:** Mean mOR level was 25.6% [38.5%], with a bimodal distribution: 10 (71.4%) subjects had low levels (2.0-9.9%), 4 subjects (28.6%) had high levels (79.9-99.4%). There was no significant association between mOR level (low vs. high or quantitative) and any subject baseline characteristic. Among the 11 subjects with repeat measurements, mOR level remained stable in all but one subject (5.8% to 97.9%), regardless of cocaine use in the interval.

**Conclusions:** Chronic cocaine users had a mean mOR closer to that previously reported for nondrug-using controls (22.8% [30.1%], n = 15) than for opiate users on methadone maintenance (47.4% [38.3%], n = 17), while having a greater proportion of subjects in the high-level group (28.6%, vs. 13.3% for controls, 52.9% for opiate users) (Zeiger et al., 2002). These findings suggest that chronic cocaine exposure may increase mOR levels on RBCs, but to a lesser extent than does chronic opiate exposure, and that the proportion of RBCs with mORs is not a good indicator of recent cocaine use.

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**EMOTIONAL ABUSE AS A RISK FACTOR FOR POOR TREATMENT OUTCOME IN RESIDENTIAL SUBSTANCE ABUSE TREATMENT.**

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**Aims:** The purpose of the current study was to examine the unique role of childhood emotional abuse, compared to physical and sexual abuse, on treatment retention among a sample of drug users entering residential substance abuse treatment.

**Methods:** 154 low income African American residents admitted to an inner-city residential drug treatment center completed the Childhood Trauma Questionnaire-Short Form to assess history of physical, sexual, and emotional abuse. Participant status was followed up with the administrative offices of the treatment center to determine the number of days they remained in treatment (continuous) and whether they completed their entire contract duration (dichotomous).

**Results:** After controlling for demographic variables, substance dependence, and Axis I comorbidity, findings indicate that participants reporting higher levels of childhood emotional abuse were significantly more likely to dropout of treatment prematurely [ $F(1,153) = 5.51, p < .05$ ], whereas physical and sexual abuse were unrelated to treatment retention. Additionally, a Cox proportional hazards regression indicated that females and individuals reporting higher levels of childhood emotional abuse had an increased likelihood of dropping out of treatment on any given day.

**Conclusions:** These findings demonstrate the need to identify symptoms associated with emotional abuse, and develop appropriate intervention programs to meet the needs of this at-risk group.

**Support:** NIDA R01 DA19405

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**NICOTINE AND LEARNING, FROM CHANGES IN BEHAVIOR TO CELL SIGNALING: IMPLICATIONS FOR NICOTINE ADDICTION.**

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**Aims:** The ability of nicotine to produce long-lasting changes in behavior contributes to the strong addictive liability of the drug. These behavioral changes are mediated by neural changes in synaptic plasticity. Nicotine has an insidious ability to facilitate maladaptive drug-stimulus associations that maintain use and facilitate relapse, while also disrupting adaptive learning. **Aims:** Examine the effects of acute, chronic, and withdrawal from chronic nicotine on contextual learning and identify the underlying neural areas, receptors, cell signaling cascades, and genes involved in the behavioral changes.

**Methods:** The effects of acute, chronic, and withdrawal from chronic nicotine on the ability of C57BL/6 and nicotinic acetylcholinergic receptor (nAChR) subunit knockout mice (n = 7-9) to learn maladaptive context-nicotine associations and adaptive context-shock associations were examined. Direct drug infusion, genetic, and molecular biological techniques were used to identify the underlying neural substrates.

**Results:** Acute nicotine facilitates both the formation of context-drug associations and context-shock associations and these associations are long-lasting. Withdrawal from chronic nicotine disrupts formation of new context-shock associations. The effects of acute and chronic nicotine involve changes in hippocampal function mediated by high affinity nAChRs and changes in cell signaling and gene expression of the mitogen-activated kinase (MAPK) family.

**Conclusions:** The effects of acute and chronic nicotine in the hippocampus are both necessary and sufficient to produce long-lasting changes in contextual learning. These changes involve altered MAPK signaling. The ability of nicotine to facilitate drug-context associations could promote context-evoked drug seeking and cravings that maintain drug use and precipitate relapse, while the ability of nicotine withdrawal to disrupt learning could also lead to relapse.

**Support:** National Institute on Drug Abuse (NIDA) (DA017949; DA024787 PI: TG); National Cancer Institute and NIDA (P5084718 PI: Caryn Lerman PhD)

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### CAN OPIATE PHARMACOTHERAPY IMPROVE VIROLOGICAL RESPONSE TO ANTI HEPATITIS C TREATMENT IN FORMER DRUG ABUSERS (INJECTING DRUG USERS)? CASE REPORT ABOUT 3 EX-IDU.

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**Aims:** Improving anti HCV treatment in ex- IDUs with severe liver diseases who had previously non response or contraindication.

**Methods:** Between 2000 and 2006, 2 men, 1 woman, aged 27, 35 and 45, with detectable serum HCV RNA (genotype 1: n=1/genotype 3: n=1/genotype 4: n=1) and with cirrhosis or extensive fibrosis (Metavir F4: n=2 / Metavir F3: n=1). One was co-infected with HIV; one had severe psychiatric co morbidity and the other one abused both alcohol and benzodiazepines in a suicidal context. All of them declared complete cessation of heroin use at least 6 months before meeting addiction medicine team. None of them were initially applying for substitution. They had standard of care follow-up for their liver disease. In one case, a first anti HCV treatment ended after 6 months because of an acute psychosis which was diagnosed to be interferon side effects. In the two other cases anti HCV therapy was denied because of psychiatric co morbidities. Patients met twice a month with addictive team. They got sublingual buprenorphine once a day (n=1) or long-lasting oral di-hydrocodeine twice a day (n=2). They were monitored with clinical interview and urinalysis.

**Results:** Their alcohol consumption decreased to less than 40 g per day. After one month of opiate treatment, pegylated Interferon and Ribavirin were introduced. All patients successfully ended their one year anti HCV treatment. Opiate treatment ended two months after anti HCV treatment cessation without relapse of heroin abuse in the year of follow-up.

**Conclusions:** More studies are needed to determine when and how to use of opiate substitution treatments. Opioids could be, in former drug injectors, part of the anti HCV treatment and improve access & adhesion to anti HCV protocols.

**Support:** Intersecteur La Terrasse. Groupe Hospitalier Maison Blanche, Paris, France.

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### HIV POSITIVE DRUG USERS LESS LIKELY TO USE CONDOMS IN SOUTH AFRICA.

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**Aims:** This study explores the association of HIV seropositivity, knowing someone with HIV/AIDS, number of sexual partners and age with condom use among men in South Africa. Knowledge of these associations will help to inform HIV prevention education in this highly HIV prevalent country.

**Methods:** The current study is cross-sectional and based on data from 410 drug users from the South African site of the International Neurobehavioral HIV Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of HIV and hepatitis A, B and C in the United States, Russia and South Africa. Data for the analysis were restricted to Black or mixed race South African males (n=176) who had confirmatory western blot HIV test results as a part of the study.

**Results:** Thirty-nine (22.7%) men in the sample tested positive for HIV; 35 (89.7%) of these 39 men reported that they had never been tested for HIV before participating in the study; and of the 4 who had been tested, only 1 man knew that he was HIV positive. The average age of the men in the study was 24 (range 18-39 years). Ninety-one (51.7%) men reported using a condom at last sex, 96 (55.4%) reported having known someone with HIV/AIDS, and 84 (47.7%) reported having had more than 5 lifetime sexual partners. Preliminary analysis suggests that South African men who were infected with HIV (OR=0.42) or knew someone who had HIV/AIDS (OR=0.51) were less likely to use condoms than men who were not infected with HIV or who did not know someone with HIV/AIDS. Age and number of partners was not associated with condom use among the men.

**Conclusions:** Our study findings suggest that HIV prevention education messages are not reaching South African men adequately. More needs to be done in South Africa to reinforce prevention for those already infected, including knowing HIV status and using condoms consistently and correctly. Future research should focus on potential reasons for inconsistent condom use and on barriers to HIV testing in South Africa.

**Support:** NIDA grants 2T32DA007292 and R01DA014498 (PI: William Latimer, Ph.D., M.P.H.).

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### ZOLMITRIPTAN AND ITS RELATIONSHIP TO THE AGGRESSION-HEIGHTENING EFFECTS OF ALCOHOL.

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**Aims:** Aggression and violence are of great concern to public health. Approximately half of murders and violent crimes occur under the influence of alcohol, as well as nearly seventy percent of domestic violence. Though the relationship between alcohol and aggression has been widely demonstrated, there is also a well-established relationship between low serotonin (5-HT) levels and high rates of aggression. However, there have been few studies examining the relationship between alcohol and 5-HT. This study looks at the interaction between alcohol and the 5-HT system as it relates to aggression. We hypothesize that the 5-HT 1B/D agonist zolmitriptan a) will mitigate the relationship between alcohol and increased levels of aggression, and b) will directly decrease levels of aggression.

**Methods:** A within-subject, counter-balanced dosing was used. Aggression was measured via the Point Subtraction Aggression Paradigm (PSAP), a well-validated laboratory measure of aggressive behavior in which subjects are provoked through monetary subtraction attributed to other individuals. Each day of testing, subjects received a drink and a capsule, with two levels of zolmitriptan (0mg, 5 mg) crossed with three of alcohol (0mg/kg, .4mg/kg and .8mg/kg) for a total of six dosing combinations.

**Results:** Four subjects have completed this ongoing study. Thus far, alcohol increased aggressive responding in all subjects under 0 mg zolmitriptan (placebo). 5 mg zolmitriptan attenuated the aggression-inducing effects of alcohol in 3 of 4 subjects. It is unclear whether zolmitriptan directly reduced aggression under 0 mg/kg alcohol.

**Conclusions:** The data provide preliminary evidence that the aggression-heightening effects of alcohol are in part mediated via the 5-HT system. Acute administration of 5-HT1B/D agonists may palliate alcohol-heightened aggression.

**Support:** NIH DA R01 003166, NIH DA R01 016965

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### THE ACETYLCHOLINESTERASE INHIBITOR DONEPEZIL MODIFIES COCAINE-INDUCED CARDIOVASCULAR AND SUBJECTIVE EFFECTS.

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**Aims:** Acetylcholinesterase (AChE) inhibitors increase synaptic levels of acetylcholine by inhibiting its breakdown, and decrease the reinforcing effects of cocaine in animals. Donepezil is an AChE inhibitor that is clinically available and relatively selective for inhibiting AChE but not other cholinesterases. Our hypothesis was that AChE inhibition would attenuate the subjective effects of cocaine.

**Methods:** We conducted a double-blind, placebo-controlled, laboratory-based evaluation of intravenous cocaine in human subjects receiving oral donepezil. Intravenous cocaine at doses of 0.0, 0.18, and 0.36 mg/kg was administered after three days of treatment with 5 mg of donepezil or oral placebo.

**Results:** Donepezil was well-tolerated. Analysis of variance showed small but significant increases in systolic blood pressure (BP) for donepezil-treated subjects that received 0.36 mg/kg of intravenous cocaine, which did not exceed 156 mm. Donepezil treatment did not modify cocaine's effects on heart rate or diastolic BP. Double-blind administration of cocaine increased self-reports of 'high', injection value, and the ARCI amphetamine subscale. For subjects receiving 0.18 mg/kg of cocaine, treatment with donepezil increased the VAS scale for 'any' drug effect without modifying self-report of 'high', craving, or the monetary value of cocaine infusions.

**Conclusions:** In summary, donepezil treatment potentiated cocaine-induced increases in systolic BP without modifying other cardiovascular effects of cocaine. Pretreatment with donepezil did not act as an antagonist for subjective effects of cocaine. Instead, treatment with donepezil increased non-specific effects of cocaine administered at a low dose, without modifying subjective effects of cocaine that are typically associated with its reinforcing properties.

**Support:** Office of Research and Development, Medical Research Service, Department of Veterans Affairs.

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### CHRONIC ANTAGONISM OF 5-HT<sub>2C</sub> RECEPTORS ENHANCE DRUG-SEEKING BEHAVIOR IN RATS TRAINED TO SELF-ADMINISTER METHAMPHETAMINE.

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**Aims:** Methamphetamine (Meth) addiction continues to be a societal problem with no FDA-approved pharmacotherapies available. Interest in the use of 5-HT<sub>2</sub> receptor antagonists to maintain drug abstinence has gained preclinical and clinical attention largely due to 5-HT regulation of dopamine. **AIM:** To ascertain the effect of chronic 5-HT<sub>2C</sub> antagonism on drug-seeking behavior.

**Methods:** On days 1-7, rats were trained to self-administer 0.1mg/kg/0.1ml infusion of Meth on a fixed ratio 1 (FR1) schedule of reinforcement for 3hrs/day. Days 8-14, rats were moved to an FR5 schedule for 3hrs/day. Day 15, drug-seeking behavior was measured by testing for cue reactivity (CR) for 1hr. CR measured the number of lever presses on an FR1 schedule in the absence of reinforcement. Immediately following this CR test (CR1), rats were allowed to self-administer Meth as on Days 8-14. Rats then underwent a 12 day period of forced abstinence during which 10 once-daily ip injections of vehicle or a 5-HT<sub>2C</sub> antagonist (SDZ SER 082, 0.3mg/kg or 1.0mg/kg) were given non-contingently in the home cage. Forty-eight hrs after the last injection, rats were tested for drug-seeking (CR2). The following day, rats received a non-contingent 0.1 mg/kg/0.1 ml infusion of Meth ("primed") and immediately underwent CR3.

**Results:** Chronic SDZ SER 082 resulted in a trend towards increased drug-seeking behavior measured in CR2 compared to vehicle, this reached significance for the 1.0mg/kg dose, tested in the Meth-primed CR3.

**Conclusions:** Chronic SDZ SER 082 increased drug-seeking behavior. This effect needs to be considered in evaluating the utility of mixed acting 5-HT<sub>2</sub> receptor antagonists (e.g., mirtazapine) to provide a lasting therapeutic benefit in the drug withdrawn addict (McDaid et al., Drug Alcohol Abuse, 86:55, 2007; Rafeyan & Napier, Society for Neuroscience Abstract, #661.1, 2008).

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### CORRELATES OF PRENATAL TOBACCO USE IN A TREATMENT SAMPLE OF PREGNANT DRUG-DEPENDENT WOMEN.

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**Aims:** The majority of pregnant drug dependent women also smoke cigarettes, and prenatal smoking is associated with a variety of adverse maternal and infant outcomes (e.g., low birth weight, prematurity). Unfortunately, smoking typically receives little attention in drug abuse treatment programs. The present study examined correlates of prenatal tobacco use in a sample of pregnant drug dependent women, with a focus on psychiatric, psychosocial and substance use severity.

**Methods:** Participants were 600 pregnant women admitted to a comprehensive residential treatment program with Cocaine and/or Opiate Dependence. Participants provided informed consent as part of a larger behavioral treatment research study and completed the Addiction Severity Index (ASI) within 3 days post-treatment enrollment.

**Results:** Current smokers (CS; n=513) obtained significantly higher ASI composite scores than non-smokers (NS; n = 87) for 2 of the 7 ASI domains (Drug Composite scores, p<.001 and Psychiatric Composite scores, p<.05). CS reported more frequent recent illicit drug use as well as a longer history of regular illicit drug use (both p<.05). Psychiatrically, CS were more likely to report suicidal thoughts both in their lifetime (p<.01) and recently (30 days pre-treatment) (p<.01). CS were also more likely to report a history of one or more suicide attempts (p<.01).

**Conclusions:** Study findings suggest pregnant drug dependent women with comorbid tobacco use present for treatment with higher illicit drug use severity and an increased likelihood of both recent and lifetime suicidal thoughts and behavior. Findings support a need for more research, with particular focus on the chronology of tobacco and illicit drug use initiation and progression and their relationship to psychiatric symptoms. Such data may inform future treatment and prevention efforts for this high-risk population of women and their children.

**Support:** Supported by the National Institute on Drug Abuse grant DA09258.

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### BUPROPION SR AND CONTINGENCY MANAGEMENT IN ADOLESCENT SMOKERS: MAIN FINDINGS.

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**Aims:** There is a significant need for evidence-based treatments for nicotine dependence in adolescents. Prior research has suggested potential roles for bupropion SR and contingency management (CM) in treatment, but no previous studies have assessed the combined effect of these interventions.

**Methods:** In a 2x2 double-blinded, placebo-controlled design, 134 adolescent smokers were randomized to receive a six-week course of bupropion SR + CM. Treatment lasted 6 weeks, with final follow-up at 12 weeks. The primary outcome was 7-day cotinine-verified point prevalence abstinence, allowing for a two week grace period.

**Results:** The combined bupropion SR + CM treatment yielded significantly superior abstinence rates throughout treatment when compared with placebo-only treatment: ORs = 5.9 (Wk 1 following grace period), 3.3 (Wk 2), 4.1 (Wk 3) and 3.6 (Wk 4; p for all <.05), but not at the final follow-up (OR = 1.8). Additionally, the combined treatment demonstrated significant superiority vs. bupropion SR only at Wk 1 (OR = 2.5), Wk 2 (OR=3.0) and Wk 4 (OR=4.1), but not at interim Wk 3 (OR=2.6) or at final follow-up (OR=2.1). Compared to CM alone, the combined group demonstrated greater efficacy at Wk 1 (OR=5.3), Wk 2 (OR=5.3), and Wk 3 (OR=3.7), but not at end of treatment (OR=3.2) or at final follow-up (OR=10.5).

**Conclusions:** Combined bupropion SR and CM may at least be efficacious in the short term (during active medication use) for smoking cessation in adolescents, and may be superior to either intervention alone. In the context of other recent findings, our results indicate need for adequately powered, randomized placebo-controlled studies to firmly establish the short and long term efficacy of pharmacotherapy, as well as combined pharmacotherapy and psychosocial treatment, for smoking cessation in adolescents.

**Support:** Supported by NIDA (R01DA17460, K12DA000357, K23DA020482) and USPHS (M01 RR 01070).

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### GEOGRAPHIC AND CONTEXTUAL FACTORS OF PRESCRIPTION OPIOID ABUSE: RESULTS FROM ASI-MV® CONNECT.

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**Aims:** Drug abuse exhibits clear geographic patterns, often associated with underlying population demographics. We aimed to determine correlations between empirical patterns of abuse and key geographic and contextual factors: drug availability, arrests for sale/possession of opioids, and residence in rural/urban areas.

**Methods:** We built on results of a latent class analysis (LCA) derived from ASI-MV® Connect, a national database of self-reported drug abuse behaviors from patients admitted to substance abuse treatment, aggregated at the 3-digit zip-code. We matched the 6-class LCA data to variables from 2007-2008 Verispan prescription sales data, 2005 US Department of Justice Uniform Crime Reports, and 2000 US Census Rural Urban Commuting Areas. Spearman or Pearson correlations and Kruskal-Wallis or ANOVA tests were conducted, as appropriate.

**Results:** The OxyContin+heroin class membership was associated with greater availability of oxycodone, more arrests for possession and sale/manufacture of opioids as well as sale/manufacture of opiates/cocaine, and they were least likely to reside in rural and small town zipcodes. Higher probabilities of class membership in the methadone class and the healthy abusers class occurred in zipcodes with increased availability of morphine and oxycodone. Poly-prescription opioid injector class membership was correlated with zipcodes exhibiting greater availability of hydrocodone, morphine, and oxycodone. The poly-prescription opioid/snorters were associated with more arrests for possession of synthetic opioids and was least likely to reside in Micropolitan zipcodes. Rural areas tended to have zipcodes with predominant prescription opioid injector and snorter classes. Prescribed misusers class membership was associated with small town zipcodes.

**Conclusions:** Important geographic and contextual associations with distinct profiles of prescription opioid abusers exist. Interventions aimed at structural level factors may hold promise for reducing abuse of prescription opioids in some areas.

**Support:** NRSA grant (TCG) from the National Institute on Drug Abuse (NIDA).

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**COMPARING GROUP PROCESS IN THE SINGLE-GENDER WOMEN'S RECOVERY GROUP VERSUS MIXED-GENDER GROUP DRUG COUNSELING.**

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**Aims:** While outcome studies have examined effectiveness of group therapy for substance use disorders, little is known about group process. Therefore, the aim of the current study is to examine the frequency of affiliative statements that represent supportive, cohesive, or empathetic connections between group members. We hypothesized that these types of statements may vary as a function of the gender composition of the group in a Stage I trial for women in a single-gender Women's Recovery Group (WRG) or in a mixed-gender control condition, Group Drug Counseling (GDC).

**Methods:** Two expert coders identified five categories of affiliative statements and developed a coding manual with acceptable inter-rater reliability. Group sessions (n=45) of WRG and GDC were coded. Cohen's effect sizes were used to determine if these statements varied significantly by treatment group, where significance is defined as a clinically meaningful difference between groups corresponding to a medium to large effect size ( $D > .5$ ). All analyses controlled for within-therapist clustering.

**Results:** Given a high level of correlation between three of the categories, Agreements, Supportive statements, and Completing Thoughts, these were collapsed into a composite category termed Empathic Statements. Empathic Statements occurred more frequently in WRG than GDC ( $D: .882$ ). However, the frequency of the remaining two statement types, Therapeutic Responses and Positive Statements About the Group, did not significantly differ between groups ( $D: -.095, -.166$ ).

**Conclusions:** One type of affiliative statements, empathic statements, occurred more frequently in the single-gender WRG than mixed-gender GDC. This is the first study to examine differences in verbal interactions among participants in all-women and mixed-gender substance abuse treatment groups. Further study is necessary to examine whether these types of group process differences mediate substance abuse treatment outcomes.

**Support:** National Institute on Drug Abuse R01 DA015434 and K24 DA019855 (SFG).

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**THE ADDICTION POTENTIAL SCALE: A VALIDATION STUDY.**

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**Aims:** Drug use is frequently under-reported for fear of negative consequences. Thus, there is a need for subtle substance use measures which can detect undisclosed drug use in high-risk populations. One such measure is the Addiction Potential Scale, an empirically-constructed substance use screener derived from the MMPI-2 (APS: Weed et al, 1992). However, the few existing studies examining the psychometric properties of the APS have yielded mixed results, rely almost exclusively on treatment samples, and use unreliable criterion measures. The aim of the current study is to examine the psychometric properties of the APS using a community sample and physiological measures of drug use.

**Methods:** A total of 183 primarily African-American women who had recently given birth were approached and asked to (1) complete a computerized assessment battery which contained the APS, and (2) provide hair and urine samples which could be used to assess recent drug use. Women completed the assessment anonymously, without knowledge of the pending request for hair and urine samples.

**Results:** For hair samples, ROC curve analysis resulted in an area under the curve of .48, which is no different from chance. Using a previously published cut-off score of 25, the sensitivity, specificity, positive and negative predictive value of the APS were .10, .90, .22 and .78, respectively. For urine samples, the area under the curve (.52) was also no different from chance. Using the same previously published cut-off score of 25, the sensitivity, specificity, positive and negative predictive value of the APS were .18, .92, .39 and .80, respectively. For both external criteria, alternate cut-scores failed to yield improvements in overall detection ability.

**Conclusions:** Despite its widespread use, the APS is not a sensitive screener for substance use in community samples. Further research is needed to identify indirect substance use screeners with better reliability and validity.

**Support:** National Institute on Drug Abuse (DA018975)

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**SUSTAINED RELEASE D-AMPHETAMINE MAINTENANCE DECREASES COCAINE SEEKING IN COC/HEROIN-DEPENDENT, BUPRENORPHINE-STABILIZED VOLUNTEERS.**

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**Aims:** BUP is effective for treating opioid but not COC dependence. Recent data suggest that d-amphetamine reduces COC reinforcement. Here we examine a dual agonist (AMP+BUP) pharmacotherapy approach for COC/heroin-dependent individuals. This ongoing human laboratory study uses a within-subject, double-blind, double-dummy design to test the hypothesis that AMP+BUP will decrease choice (drug combination vs. money) progressive ratio responding for COC alone (100mg IN + saline IM) or COC with hydromorphone (HYD 24mg IM) vs. HYD alone (with 4mg COC placebo) and dual placebo; and decrease COC subjective effects but not potentiate its physiological effects.

**Methods:** Non-treatment volunteers with current COC abuse or dependence and opioid dependence (DSM-IV) are stabilized on BUP 8 mg/day throughout the study. During a 3-week inpatient stay, subjects are maintained on ascending oral doses of AMP, given twice daily (0730 and 1230): placebo (0mg BID), 15mg BID (30mg/day), and 30mg BID (60mg/day) during weeks 1-3, respectively. Each week, after 3 days AMP stabilization (Sat-Mon), 4 sessions (Tue-Fri) occur in randomized order. Subjects sample the COC-HYD dose combination at 0900 (effects measured until 1200); make drug vs. money (\$2) choices from 1230-1530; and receive response-contingent drug at 1530.

**Results:** Preliminary results are from 4 completers. Relative to placebo, AMP 30mg/day and 60mg/day reduce COC choices ( $M_s = 6.0, 2.5$  and  $2.8$ ),  $F(2,6) = 3.89$  ( $p=.08$ ) and breakpoints ( $M_s = 1704, 416$  and  $523$ ), but not COC+HYD choices or breakpoints. Both AMP doses reduce COC peak ratings of VAS 'want drug again' (e.g.  $M_s = 63, 18$  and  $18$ ), 'liking' and 'stimulated', and COC craving but are not potentiating COC heart rate or blood pressure responses.

**Conclusions:** These preliminary data show that AMP (vs. placebo) + BUP reduces COC seeking. If this pattern persists it would suggest that, in subjects for whom AMP is safe and well tolerated, there are selective effects on COC-reinforced behavior and indices of abuse liability.

**Support:** NIH R01 DA022243 and Joe Young, Sr. Funds (State of Michigan)

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**SUSTAINED ABSTINENCE IN ADOLESCENCE IS ASSOCIATED WITH FUTURE ECONOMIC WELL-BEING AMONG HIGH-RISK ADOLESCENTS.**

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**Aims:** The stated goal of most substance abuse treatment is to achieve sustained abstinence. Sustained abstinence, however, is defined differently across studies and there is mixed evidence as to whether it leads to favorable long-term outcomes. This study investigates the relationship between sustained abstinence during adolescence and economic and academic outcomes in young adulthood.

**Methods:** The sample includes former juvenile offenders enrolled in 1 of 7 group homes in Los Angeles between 1999 and 2000 and followed up at 3, 6, 12, 72, and 87-months post-enrollment. Propensity score weighting was used to ensure comparability between our abstinent and non-abstinent groups. Our primary outcomes included total legitimate income, financial instability, educational attainment, and rates of institutionalization at the 87-month follow-up.

**Results:** At 87-months post-intake, youth with 12-months of sustained abstinence had on average \$1,465 more in legitimate earnings in the past 90 days than youth who were not abstinent (95% CI = \$325, \$2605); they were 1.6 times more likely to obtain their GED or high school diploma by the age of 20 (95% CI = 0.9, 2.9) and half as likely to be institutionalized (95% CI = 0.3, 1.0). Youth who abstained from only hard drugs were not significantly different than hard drug users on these 3 outcomes. However, abstainers from hard drugs had significantly lower rates of financial instability than hard drug users. Finally, 12-month abstainers were 2.3 times more likely to receive their GED or high school diploma than 6-month abstainers (95% CI = 1.1, 5.0) and earned on average more than \$1500 more (95% CI = \$610, \$2553). There were no statistically significant differences between 6-month abstainers and users.

**Conclusions:** Periods of sustained abstinence in this sample lead to higher rates of educational attainment, higher earnings, and lower likelihoods of being institutionalized. The keys to the favorable effects of abstinence appear to be abstinence from all substances and to having periods of sustained abstinence at least as long as 12-months.

**Support:** NIDA - 5R01DA016722-04

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**DIFFERENCES IN D2 RECEPTOR AVAILABILITY IN HIGH AND LOW IMPULSIVE MONKEYS.**

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**Aims:** Individual variation in behavioral impulsivity, and proposed underlying cognitive endophenotypes, are thought to represent vulnerability factors for substance abuse, but the molecular basis of impulsivity remains unknown. Stimulant dependent individuals exhibit lower D2 receptor availability in the striatum and low D2 receptor binding correlates with an impulsive phenotype and drug abuse liability. These results suggest that cognitive control and impulsivity may share a common neural mechanism that may be mediated by the D2 receptor. This study examined the association of D1 and D2 receptor availability with impulsivity and a measure of cognitive control.

**Methods:** 10 vervet monkeys were selected from their birth cohort based on an impulsivity score derived from the Intruder Challenge Task. 5 high scoring monkeys comprised the high impulsivity group and 5 low scoring animals comprised the low group. Monkeys received a single PET scanning session with [<sup>11</sup>C] NNC-112, to assess D1 receptor availability, and [<sup>18</sup>F] Fallypride to assess D2 receptor availability. Binding potentials were calculated and extracted using ROIs drawn on corresponding MRIs. Behavioral flexibility was assessed using a three choice discrimination acquisition/reversal task.

**Results:** High impulsive monkeys had significantly greater D2 receptor availability in the left caudate, right caudate, left nucleus accumbens and right nucleus accumbens. No differences were found in D1 receptor availability or in cortical regions for either NNC-112 and Fallypride. High impulsive animals required more trials to reach criterion for the initial acquisition phase.

**Conclusions:** These results demonstrate dopaminergic correlates of individual variation in an ethologically-valid measure of impulsivity. Differences in discrimination learning may indicate a general deficit in attentional processes involved in the cognitive control of discrimination learning. Together, these results further demonstrate an important relationship between striatal D2 receptors and impulsivity.

**Support:** P50-MH77248  
RL1-83270

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**TREATMENT ENTRY AMONG INDIVIDUALS ON A WAITING LIST FOR METHADONE MAINTENANCE.**

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**Aims:** Demand for publicly-funded methadone treatment outpaces supply in many areas of the United States, resulting in waiting lists for care. During the waiting period, the benefits of treatment for individual and public health remain unrealized. This study utilized the wait list control sample from a randomized clinical trial of interim methadone maintenance to examine predictors of treatment entry.

**Methods:** Heroin users on a waiting list for methadone treatment (n=120) were assessed with the Addiction Severity Index, the T.C.U. Motivation Scale and a Waiting List Questionnaire at study entry and at 4 month follow-up. Logistic regression was used for the analysis. We hypothesized that, controlling for baseline characteristics, (a) intravenous drug users would be more likely to enter treatment than intranasal users, (b) cocaine users would have lower likelihood of entering treatment, (c) higher motivation for treatment would be predictive of entry, and (d) cocaine use would moderate the effects of motivation on treatment entry.

**Results:** Only 25 individuals (20.8%) entered treatment within four months of being placed on a waiting list. Controlling for age, sex, social connectedness, previous treatment episodes, and incarceration history, our first two hypothesis were supported in that intravenous drug users were more likely to enter treatment ( $p<.05$ ) whereas cocaine users were less likely to do so ( $p<.01$ ). We did not find support for the latter two hypotheses. While the sample as a whole was a motivated group, the level of individual motivation for treatment appears to have had little effect on the outcome.

**Conclusions:** The low probability of actually entering treatment from the waiting list is alarming. The higher likelihood of treatment entry among intravenous users provides some encouragement from a public health standpoint, although programs may need to make special efforts to facilitate entry for treatment-seeking heroin users who also use cocaine.

**Support:** R01 DA 13636 (PI: R.P. Schwartz)

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**IMPULSIVITY IS CORRELATED WITH WHITE MATTER ALTERATIONS IN CHRONIC MARIJUANA SMOKERS.**

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**Aims:** Difficulties in the ability to monitor and inhibit impulsive behaviors have been reported in marijuana (MJ) users, and neuroimaging studies of frontal systems in MJ smokers report alterations during inhibitory tasks. Diffusion tensor imaging (DTI) provides a quantitative estimate of white matter integrity, offering new insight at the microstructural level. We applied DTI, clinical ratings and impulsivity measures to test the hypotheses that MJ smokers would show alterations in white matter relative to controls and exhibit a different pattern of association between white matter and impulsivity measures.

**Methods:** Fractional anisotropy (FA), a measure of directional coherence and integrity of white matter fiber tracts, was calculated for bilateral frontal regions placed anterior and lateral to the frontal horns in 15 chronic MJ smokers and 15 controls. Subjects also completed the Positive and Negative Symptom Scale (PANSS), Profile of Mood States (POMS), Beck Depression Inventory (BDI), Hamilton Anxiety Scale (HAM-A), and the Barratt Impulsivity Scale (BIS).

**Results:** As hypothesized, analyses revealed significant reductions in left frontal FA in MJ smokers relative to controls ( $F=4.43$ ;  $p=.044$ ). Despite no significant between-group differences for any mood rating, MJ smokers had significantly higher BIS scores, both for total ( $F=6.54$ ;  $p=.019$ ) and BIS motor subscale ( $F=6.71$ ;  $p=.018$ ). Interestingly, a significant relationship was detected between these measures and left frontal FA values in MJ smokers (BIS total  $r=.700$ ;  $p=.024$ ; BIS motor  $r=.663$ ;  $p=.037$ ) but not controls.

**Conclusions:** These data represent the first report of significant alterations in frontal white matter fiber tract integrity which are associated with impulsivity measures in chronic MJ smokers. Findings suggest that white matter changes are associated with increased impulsivity, and may contribute to initiation of MJ use or an inability to discontinue. The relationship of these measures to toxicology and age of onset of MJ use will be considered.

**Support:** NIDA R21 and R03 to Dr. Gruber

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**LEGALIZATION OF MARIJUANA USE IN MEXICO.**

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**Aims:** To analyze the recent proposals to legalize the use of marijuana in Mexico.

**Methods:** Analysis of the proposals presented to state and national congress by some representatives (diputados).

**Results:** Criminality and insecurity are the major concerns among in the Mexican society nowadays. Several representatives (diputados) from left wing or opposition parties, have been proposing legalization of marijuana as a way to curb violence and crime associated with the drug trafficking. The proposals have been presented both to the media and state and national Mexican Congress. They share in common an initiative for a Treatment program or "Coordinating Center" for drug users and include the decriminalization of carrying an amount of drug for personal use. Other initiatives propose to legalize production, sale, and distribution of marijuana and even allow to cultivate plants at home. Another proposal includes "health education" sanctions to drug users.

All the proposals include the view of considering users as drug addicts and not criminals; some of them go as far as proposing crop and distribution licenses, sole vendors and market regulation. None include norms or guidelines for it use, leaving them for the health authorities and government agencies in general to develop.

**Conclusions:** There seems to be a partial and incomplete approach to the problem. It is evident that the proposals are abundant in historical and pro marijuana notes and references but, as a rule, lack citations and references on health and psychological effects of marijuana. Moreover, there is a complete absence of references from sources such as scientific journals nor from organizations such as NIDA or PND (Spain) not to mention Mexican sources of information.

**Support:** University of Guadalajara, Consejo estatal contra las adicciones en Jalisco.

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**ADDRESSING NICOTINE DEPENDENCE IN DRUG TREATMENT SETTINGS: ORGANIZATIONAL CHANGE.**

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**Aims:** Addressing Tobacco Through Organizational Change (ATTOC) is a manualized intervention to guide drug abuse treatment programs in addressing comorbid nicotine dependence. This study implemented ATTOC in each of three residential programs.

**Methods:** Staff and clients were surveyed, pre and post intervention, on smoking knowledge, beliefs about treating smoking, self-efficacy in delivering such treatment (staff only), smoking services provided/received, and barriers to smoking cessation. Staff at pretest (n= 114) had a mean age of 45, 75% were female, 42% were smokers and 65% were in recovery. Clients at pretest (n=150) had a mean age of 35, 58% were female, and 85% were smokers.

**Results:** In two clinics where data collection is complete, mean scores (knowledge, beliefs, barriers, self-efficacy, practices) were compared in ANOVA with factors for clinic, time (pre/post), and their interaction. Among staff, beliefs about providing smoking cessation services improved pre to post (p=.0008), as did self-efficacy in addressing smoking with clients (p=.0053), and smoking-related practices provided by counselors (p=.0363). Mean scores for clients increased in terms of the amount of smoking-related services received (p<.05), and beliefs about including smoking cessation in drug abuse treatment were more positive (p<.0001) following the intervention. Data from the third study site will be incorporated into analyses shortly, offering a more complete picture of intervention effects.

**Conclusions:** The ATTOC intervention was effective in changing staff and client beliefs about smoking, and increasing the amount of smoking-related services provided. Differential implementation of the intervention by site and erosion of intervention effects over time were observed. The ATTOC intervention can initiate change in smoking-related program policies and practices, but additional policy support (local, state, national) may be needed to maintain those changes.

**Support:** NIDA R01 DA020705, P50 DA09253, U10 DA15815.

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**LONGITUDINAL CHANGES IN ATTACHMENT, SOCIAL SUPPORT, PARENTING ATTITUDES, AND PSYCHOLOGICAL FUNCTIONING AMONG WOMEN DRUG ABUSERS.**

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**Aims:** Our study involves women drug abusers in community treatment. We hypothesized that: subjects (Ss) would show extensive disruption in their attachment, social support, and psychological functioning; Ss who attended treatment longer would show greater improvement in functioning; and Ss who attended women-focused treatment would show greater improvement in their adult relationships, social support, psychological functioning, and parenting.

**Methods:** Instruments included: Experiences in Close Relationships Inventory, ISAP social support scale, Brief Symptom Inventory, and Adult-Adolescent Parenting Inventory. Sample: 300 female drug abusers in mixed gender and women-focused treatment.

**Results:** At baseline, Ss showed levels of attachment anxiety and avoidance of intimacy greater than women in normative samples. Ss' parenting scores were far below normative samples. Preliminary analysis (n=242) shows significant improvements in adult attachment anxiety, social support, and a trend toward improved psychological functioning. But, parenting attitudes did not change over time. Social support at 12 months was associated with days in treatment, however, type of treatment did not predict 12-month scores on any scales. Results may change as data from all Ss become available.

**Conclusions:** Preliminary results indicate that few participants had secure attachment styles. While attachment styles changed over time, the move was not toward a secure attachment style. Ss showed improvement in social support and psychological symptoms. Given the cyclical nature of abuse, the lack of improvement in parenting attitudes over time shows a high need among this population for additional parenting intervention. If preliminary results are borne out in the full sample, women-focused treatment may not produce superior outcomes in the areas of parenting, adult attachment and social support, and psychological functioning.

**Support:** This study is funded by National Institute of Drug Abuse grant R01DA016277-01.

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**SOCIAL NETWORK CORRELATES OF UNPROTECTED SEX IN RUSSIAN INJECTION DRUG-USING SEXUAL PARTNERSHIPS.**

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**Aims:** Russia's HIV epidemic is among the fastest growing worldwide. Historically driven by IDUs, the Russian HIV epidemic is spreading into the general population. Sexual contact is becoming an important transmission route with high-risk individuals acting as potential 'bridges.' Determinants of sexual risk among IDUs must therefore be elucidated to inform prevention strategies. The correlates of unprotected sex in the sexual partnerships (dyads) of Russian IDUs are examined at the individual, dyad, and network level.

**Methods:** IDUs (N=502) were recruited in St Petersburg, Russia, for a network HIV prevention intervention (12/2004-04/2008). GEE models were used to assess associations with unprotected sex within sexual partnerships (dyad N=645).

**Results:** Of the dyad-level characteristics, receptive syringe sharing with the sexual partner, social exposure (hanging out with network member [NM], seeing NM daily, living with NM), and being HIV concordant (both the participant and the NM were reported being HIV+) were associated with unprotected sex, while HIV discordant couples (one reported HIV+ and the other HIV-) were less likely to have unprotected sex. No individual-level or social network-level variables were significant.

**Conclusions:** There is a combined risk of unsafe injecting and unsafe sexual behaviors among Russian injecting dyads. Both these risks domains must be addressed simultaneously in interventions that target the injecting partnerships of IDUs to reduce the spread of HIV in Russia. Free and confidential HIV testing is also critically needed for all IDUs, and regular HIV testing combined with couples counseling should be available for those IDUs who are both injecting and sex partners.

**Support:** R01 DA016142

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**METHAMPHETAMINE-RELATED VIOLENCE AMONG WOMEN USERS.**

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**Aims:** Little systematic attention has been paid to the relationship between methamphetamine (meth) use and violence. Violence perpetrated by women who use meth is essentially unheard of in the scientific literature. The aim was to explore women users' experiences with meth-related violence in order to begin to conceptualize how meth contributes to violence, with special emphasis on how violence manifests in women meth users.

**Methods:** Thirty meth-dependent women in residential treatment completed in-depth interviews about their life experiences and perspectives on the impact of meth on their behavior, including violent behavior (perpetrated against as well as by them). The average age of the participants was 28 years; 56% Latina, 30% white, 7% Native American, and 7% mixed.

**Results:** Eighty percent (n=24) reported experiencing violence: 67% (n=20) had violence perpetrated against them, 57% (n=17) had perpetrated violence against their partners or others (e.g., family members). Most of the women who perpetrated typically did so while "coming down" off of meth and blamed their violent behaviors on the meth, but 30% (n=10) explicitly described pre-existing "anger issues" that were exacerbated by meth. The majority did not typically become violent defensively (e.g., to protect themselves or their children) but, rather, instigated violence within the context of intimate relationships, drug-related networks, families, or criminal activities. Violence between intimate partners was in some cases related to sexual issues attributed to meth.

**Conclusions:** Although male-perpetrated domestic violence was reported, more than half of the participants (57%) reported perpetrating violence. It is well-known that meth can affect executive function and decision-making, especially in women. The question of whether meth causes violence or disinhibits pre-existing violent tendencies or both remains unanswered at this time. Considering the increase in meth use nationwide, especially among women, this question deserves further investigation.

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**ARE THERE COGNITIVE SEQUELAE TO CALLOSAL DAMAGE IN CHRONIC COCAINE USERS?**

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**Aims:** Recent investigations have demonstrated a significant decrease in corpus callosum integrity in chronic cocaine users. As the largest white matter pathway in the brain, the callosum is essential for complex cognitive tasks which require integration of information from both the left and right hemisphere. The purpose of the current investigation was to determine the extent to which compromised callosal integrity is associated with cognitive deficits in cocaine users.

**Methods:** Diffusion tensor imaging data was acquired from chronic cocaine users and matched controls that performed a standardized cognitive assessment battery (CANTAB). Linear discriminant analysis isolated the components of the CANTAB that maximally differentiated cocaine users from controls. A region of interest analysis was subsequently used to determine the extent to which these outcome measures correlated with DTI measures of white matter integrity in the corpus callosum.

**Results:** Total errors on the attentional set-shifting and action planning tasks were the strongest predictors of group membership, with cocaine users impaired on both tests. Overall, cocaine users had lower white matter integrity (fractional anisotropy or FA values) than controls. Furthermore, users with higher integrity or FA values along the callosum were less impaired than those with more degradation ( $p < 0.05$ , corrected).

**Conclusions:** These data, then, confirm and integrate findings of previous reports showing cognitive deficits or loss of white matter integrity in cocaine users. The significant correlation between cognitive performance and corpus callosum integrity suggests the importance of interhemispheric processing in the functional status of cocaine users.

**Support:** These investigations were supported by grants DA021456 (CAH), DA20074 & DA06634 (LJP) from NIDA.

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**PREVALENCE AND FACTORS ASSOCIATED WITH HCV POSITIVE SALIVA TEST IN INJECTING DRUG USERS IN NORTH AND EAST FRANCE.**J Harbonnier<sup>1,2</sup>, E Lavie<sup>3</sup>, Marc Auricombe<sup>3</sup>, <sup>1</sup>Centre Boris Vian, Lille, France, <sup>2</sup>North and East IVDU HCV Study Group, Lille, France, <sup>3</sup>Addiction Psychiatry, Université de Bordeaux, Bordeaux, France

**Aims:** To assess prevalence and associated risk factors of HCV infection among injecting drug users with last HCV testing negative or unknown, in 18 addiction treatment centers in North and East France.

**Methods:** Recruitment took place from January to April 2008. Inclusion criteria were: aged 18 or more, having used the IV route at least once lifetime, HCV serology negative or unknown. Subjects were tested for HCV antibodies on saliva with Monolisa method, and in case of positivity, blood samples were tested for HCV antibodies and HCV RNA with a polymerase chain reaction method. Physician in charge reported information about each subject: age, sex, venous status (normal, impaired or very impaired), first and last injection date, and date of last HCV testing.

**Results:** 262 subjects were included (81% males, median age 30 y.). 222 (85%) were in buprenorphine (68) or methadone (154) treatment. 98 (38%) had never had HCV testing. 15 subjects (5.7%, 14 males) tested HCV positive on saliva, 6 (2.3%) were confirmed on RNA analysis and for the other 9 blood samples were not available. In univariate analysis, HCV positive subjects were older (39 vs. 30,  $p < 0.001$ ), started use of IV route earlier (1991 vs. 2000,  $p < 0.001$ ), HCV status before the study was more often unknown (67% vs. 36%,  $p < 0.05$ ) and venous status was more often impaired (80% vs. 43%,  $p < 0.01$ ). In multivariate analysis, starting use of IV route before 1992, impaired venous status and unknown HCV serology status were associated with increased risk of HCV positivity in saliva.

**Conclusions:** Most of those that tested HCV positive started the IV route before 1992 and very few that started more recently were positive. This may be related to HCV related harm-reduction strategies.

**Support:** Roche Pharmaceuticals, France.

The North and East France HCV IVDU Study Group: A. Decoster, D. Lucidarme, D. Fremaux, C. Jacob, A.F. Hirsh, P. Josse, P. Schillé, C. Richez, O. Pouclet, S. Suquet, N. Messaadi, R. Semal, N. Heyrès, C. Vasseur, A. Muysen, B. Filoche.

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**REDUCTION OF ADDICTION SEVERITY IN ALCOHOL AND DRUGS: A BIVARIATE MULTILEVEL MODELING APPROACH.**Motoaki Hara<sup>1,2</sup>, Y Huang<sup>1</sup>, Y Hser<sup>1</sup>; <sup>1</sup>Integrated Substance Abuse Programs, University of California, Los Angeles, Los Angeles, CA, <sup>2</sup>Graduate School of Education and Information Studies, University of California, Los Angeles, Los Angeles, CA

**Aims:** To identify client- and program-level factors contributing to the simultaneous reduction of Addiction Severity Index (ASI) sub-scale scores in alcohol and drug for residential and outpatient drug free treatment.

**Methods:** Data are based on 1,468 individuals (1,045 males and 423 females) who participated in the Treatment System Impact study, a multi-site prospective study designed to investigate the impact of Proposition 36 on client treatment outcomes. Bivariate multilevel model is applied to jointly examine the impact of contributing factors at both client and program levels on the reduction of problem severity in alcohol and drug use from intake to the 12-month follow-up.

**Results:** Univariate multilevel analysis of ASI Alcohol subscale identifies being in residential treatment, longer drug use history, being a male subject, and lower number of felony counts as significant predictors of effective reduction in alcohol addiction severity. A separate univariate multilevel model of ASI Drug subscale identifies ASI scores in Alcohol, Family, Legal, Medical and Psychiatric domains at intake, as well as treatment modality to be significant predictors of drug addiction severity reduction. However, a bivariate multilevel model, which jointly analyzes these two outcomes, identifies the intake ASI score in Alcohol and Legal domains for reduction in alcohol addiction severity, and the intake Drug and Psychiatric ASI scores for the reduction of drug addiction severity. Notably, treatment is less effective amongst females for both outcomes. The number of past felony convictions is predictive of less favorable outcomes.

**Conclusions:** Simultaneous estimation of alcohol and drug addiction severity sheds light on the underlying treatment mechanism unattainable under univariate outcome models.

**Support:** P30 DA016383, K05DA017648, and T32 DA07272-16A1 from the National Institute on Drug Abuse.

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**THE EFFECTS OF IV PRENATAL TETRAHYDROCANNABINOL EXPOSURE ON PASSIVE AVOIDANCE PERFORMANCE IN MALE AND FEMALE JUVENILE RATS.**

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**Aims:** We wished to examine the effects of prenatal exposure to two different doses of THC, the main psychoactive component in marijuana, on learning and memory during the juvenile period.

**Methods:** Pups were exposed to a high (.3 mg/kg) or a low (.15 mg/kg) dose of THC or the pluronic acid vehicle via IV injections given every 3 days to the dams. As an additional control, we compared these pups to a group of non-treated pups. Beginning on postnatal day 22, pups' acquisition of the shuttle-box passive place avoidance task, 1-hour, 24-hour and 1-week retentions were tested. The task consisted of a 3-minute habituation trial followed by 5 3-minute acquisition trials where the latency to enter the dark chamber (and receive a shock) was recorded.

**Results:** There were no significant sex or treatment differences in the acquisition of the passive avoidance task. All rats learned to avoid the shock by the 5th trial. Data for the 1-hour and 24-hour retention intervals were variable and showed no significant differences between groups and sexes. However, at the 1-week retention interval, female treated rats showed improved retention compared to female control rats. In male rats at 1 week, only non-treated males showed greater retention than treated males. Additionally at the 1-week retention interval, female treated rats exhibited greater retention of the passive avoidance task compared to male treated rats.

**Conclusions:** These results indicate that prenatal exposure to THC affects retention of a passive avoidance paradigm, and that females appear to be more sensitive to these effects than males.

**Support:** Studies were supported by NIH grant RO1 DA019348

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### THE RELATIONSHIP BETWEEN RESPONSE TO LABORATORY STRESS PROVOCATION AND RELAPSE TO COCAINE.

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**Aims:** Stress plays a significant role in vulnerability to relapse among individuals with substance use disorders. However, the precise mechanisms connecting stress and relapse are not well understood. In this study, the relationship between reactivity to three human laboratory stress paradigms and cocaine was explored.

**Methods:** Participants included 47 (23 men, 24 women) cocaine-dependent individuals. Subjects completed the Trier Social Stress Task (i.e., performed a speech and math calculations in front of an audience), a pharmacological stress provocation (i.e., administration of corticotrophin releasing hormone; CRH), and a cocaine cue exposure paradigm after an overnight hospital stay. Biological markers, including cortisol, adrenocorticotrophin hormone (ACTH), heart rate and blood pressure as well as subjective measures of cocaine craving and stress were assessed at baseline and at several time points post-tasks. Participants' cocaine use, including time to first use and amount used per using day were assessed for one month following testing.

**Results:** In response to the drug cue exposure and CRH, craving and stress were significant predictors of cocaine use during the follow-up period. Heart rate, but not neuroendocrine response to CRH was a significant predictor of cocaine use. In contrast, neuroendocrine responses to the Trier were most predictive of cocaine use.

**Conclusions:** These findings demonstrate that subjective, physiologic and neuroendocrine reactivity to laboratory paradigms can predict subsequent cocaine use. The predictors vary based on the type of provocation employed. Interventions aimed at attenuating stress-related parameters may prove useful in helping to prevent relapse.

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### SUPPORTING OPPORTUNITIES FOR ADOLESCENT RECOVERY.

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**Aims:** Special Service for Groups/Homeless Outreach Program's Supporting Opportunities for Adolescent Recovery (SOAR) will provide evidence-based, family-centered substance abuse treatment to 102 minority, low-income, substance-abusing male youth ages (12 to 20) and their families in South Los Angeles, California over three years. The goal of SOAR is to increase access to evidence-based family-centered substance use treatment for youth. To achieve this goal, the project has the following objectives: (1) increase rates of abstinence from alcohol and drugs, (2) increase rates of social connectedness, (3) and decrease trajectories toward delinquent behaviors.

**Methods:** A cohort of 25 participants were interviewed at baseline, and then participated in two interventions: the Adolescent Community Reinforcement Approach (ACRA) and the Assertive Continuing Care (ACC); they were interviewed again at three months follow-up.

**Demographics for this sample were:** 25 males; Hispanic (60%) or African American (40%); 15-17 years (59%), 18 or over (34%) and less than 15 years (7%). Some of their risk factors included being a high school drop-out, unemployed with no income, gang-affiliated, abusing drugs and alcohol, and on probation and/or court ordered to obtain treatment. The 3 month follow-up rate was 72%.

**Results:** Preliminary results (from baseline to 3 month follow-up) revealed that: rates of abstinence from alcohol and drugs increased from 44.4% to 61.1%; rates of social connectedness increased from 35.3% to 76.5%; rates of Crime and Criminal Justice (had no past 30 day arrests) increased from 83% to 89%; rates for currently attending school or employed increased from 79% to 83%.

**Conclusions:** These findings suggest that SOAR can be effective at fostering positive social networks among high-risk youth, and is also instrumental in reducing substance use and related problems.

**Support:** HHS/SAMHSA/CSAT #T117646

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### ADOLESCENT METHYLPHENIDATE TREATMENT AUGMENTS LATER VULNERABILITY TO COCAINE ADDICTION IN RATS WITH AN ADHD PHENOTYPE.

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**Aims:** A dysfunctional prefrontal cortex underlies not only cocaine addiction, but also ADHD, which are often co-morbid. Disagreement remains concerning use of methylphenidate (MPH) and whether it renders individuals with ADHD more vulnerable or less vulnerable to later cocaine addiction. A rat strain exhibiting an ADHD phenotype may be useful, as investigating this issue only in rats lacking an ADHD phenotype may not be as informative.

**Methods:** From P28-P55 (adolescence), rats of the SHR and WKY strains received oral MPH (1.5mg/kg) or vehicle (n=4-6). Beginning on P35, rats were tested for attention in a visual discrimination task. Beginning on P77 (adulthood), acquisition of cocaine self-administration, FR dose-response curves, and PR breakpoints were determined.

**Results:** During adolescence, never-medicated SHR made ~3-fold more errors to reach the learning criterion compared to never-medicated WKY (p<0.005). MPH treatment prevented attention deficits in the SHR. MPH treatment also improved attention in the WKY who made ~2-fold less errors than never-medicated WKY (p<0.04). During adulthood, never-medicated SHR acquired cocaine self-administration faster (p<0.05) and had a higher PR breakpoint (p<0.04) compared to both WKY groups. MPH-treated SHR, in addition to acquiring cocaine self-administration faster than both WKY groups (p<0.05), displayed a significant (p<0.05) upward shift in the inverted U-shaped dose-response curve for self-administered cocaine and a higher (p<0.01) PR breakpoint than both WKY groups as well as the never-medicated SHR.

**Conclusions:** Co-morbidity between ADHD and cocaine addiction is reproduced in this animal model. Moreover, cocaine addiction vulnerability is further enhanced in rats with an ADHD phenotype following discontinuation of MPH during adulthood. As adolescence represents the age at which initiation of stimulant ADHD medications may more easily transform into later substance use disorders, these findings underscore the appropriateness of using a rat strain with an ADHD phenotype to model co-morbidity between ADHD and cocaine addiction.

**Support:** Supported by DA11716

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### FACTORS ASSOCIATED WITH HEPATITIS C SEROPOSITIVITY AMONG INCARCERATED WOMEN RE-ENTERING THE COMMUNITY.

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**Aims:** Hepatitis C (HCV) infection is more prevalent within correctional settings than in the general population. Therefore, the purpose of this analysis was to determine the factors associated with HCV infection among female inmates re-entering the community.

**Methods:** Participants consisted of women age 18 and older who were part of the CJ-DATS Reducing Risk Relationships for HIV (RRR-HIV) study. This multi-site randomized trial examined the efficacy of a six-session behavioral intervention on reducing HIV and HCV risk behaviors and increasing knowledge of the risk factors for transmitting infection among incarcerated women re-entering the community. Of the 444 women completing the baseline questionnaire, 419 (94.4%) submitted to HCV testing. Contingency table analysis and multivariable logistic regression were used to determine factors associated with HCV infection.

**Results:** The majority of women were white (71.9%) and the median age was 34.6 years (IQR: 27.6, 41.7). In the 30 days prior to incarceration, women most commonly reported using crack (36%), alcohol (27.8%) and prescription opiates (27.3%). Adjusting for age, race, study site and randomization status, lifetime injection drug use (IDU) was associated with HCV infection (adjusted odds ratio [AOR]: 18.7, 95% CI: 9.7, 36.2), as was a history of blood transfusion(s) (AOR: 4.2, 95% CI: 1.7, 9.8). Interestingly, having one or more tattoos was a protective factor for HCV infection (AOR: 0.3, 95% CI: 0.1, 0.6).

**Conclusions:** In this analysis among female inmates re-entering the community, it was found that lifetime IDU was strongly associated with HCV infection. Given these findings, preventing reuptake or initiation of IDU upon release for both HCV seropositive and seronegative women is of the utmost importance in order to prevent transmission of the virus. Interventions aimed at preventing IDU and other risk factors are therefore warranted among women re-entering the community.

**Support:** U01DA016205



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**GENDER DIFFERENCES AT PRESENTATION FOR TREATMENT-SEEKING OPIATE DEPENDENCE.**

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**Aims:** Significant gender differences in substance use disorders have been reported in the literature. Little is known, however, with regard to gender differences in patients presenting with opiate dependence. This secondary data analysis examined demographic and baseline substance use characteristics of 935 (305 women, 630 men) seeking outpatient treatment for opiate dependence.

**Methods:** Participants were screened for the NIDA-sponsored Clinical Trials Network (CTN) 0003 study of suboxone taper schedules. A comprehensive battery of instruments was administered, including the Addiction Severity Index-Lite, Adjective Rating Scale for Withdrawal (ARSW), Clinical Opiate Withdrawal Scale (COWS), and a visual analog scale for craving (VAS).

**Results:** Men were significantly older than women [36.43(SD=10.7) vs. 34.71(SD=9.5) yrs,  $p=.03$ ] at baseline. In addition, men evidenced significantly higher alcohol ( $p=0.002$ ) and legal ( $p=0.006$ ) ASI-Lite composite scores. In contrast, women had significantly higher drug ( $p=0.0004$ ), employment ( $p=0.0007$ ), family ( $p<0.0001$ ), medical ( $p=0.0005$ ), and psychiatric ( $p<0.0001$ ) ASI-Lite composite scores. Women also reported significantly higher baseline craving for opiates ( $p=0.001$ ). No significant gender differences in presenting opiate withdrawal symptoms were revealed.

**Conclusions:** The findings demonstrate significant gender differences in presenting substance use severity, craving for opiates, as well as other areas of functioning. The observed differences may have important implications for gender-specific treatment design and implementation.

**Support:** NIDA Clinical Trials Network (5U10DA013727)

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**ASSOCIATIONS BETWEEN SEXUAL RISK BEHAVIOR PATTERNS AND HIV IN FEMALE SOUTH AFRICAN DRUG USERS.**

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**Aims:** South Africa is in the center of the global epidemic of HIV with female South Africans most vulnerable to infection (UNAIDS, 2006; WHO, 2006). Furthermore, drug users are at particular risk in South Africa due to the vulnerability of this population to high risk sexual behaviors during and as a result of substance use (Parry et al. 2008; Parry et al. 2008; Sawyer et al. 2006). Therefore, patterns of sexual risk behaviors were explored in a cross sectional sample of 200 South African female drug users recruited in the Pretoria region of South Africa in order to determine whether particular behaviors co-vary in subpopulations using a Latent Class Analysis.

**Methods:** Once sexual risk behavior classes were determined, classes were used in a model to predict HIV. Sexual risk behaviors included: sexual debut before age 15, whether or not first sexual debut was with a risky partner, sex trade, condom use in last sexual encounter, lifetime casual partner and current steady partner. Results of the LCA demonstrated a three class solution with optimal fit deduced by Bayesian Information Criterion minima.

**Results:** The three classes included: a low sexual risk class with no sex trade (class 1: 19%) and low probability of sexual risk behaviors, a high sexual risk class with sex trade and more frequent endorsement of condom use and less frequent endorsement of ever had a casual partner (class 2: 55%) and a high sexual risk class with sex trade and less frequent endorsement of condom use and more frequent endorsement of ever had a casual partner (class 3: 26%). Furthermore, a logistic regression analysis of HIV using class membership as the main covariate while controlling for age, education and drug use indicated that that for participants in class 3, HIV infection was 3.13 (95% CI= 1.09, 8.96) the odds of participants in class 1.

**Conclusions:** Findings have implications for the prevention of HIV in female South African drug users by changing patterns of negatively co-occurring sexual risk behaviors.

**Support:** The study authors would like to acknowledge NIDA T32DA007292 and R01DA014498.

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**USING WEB-BASED TECHNOLOGY TO ENHANCE PRACTICAL APPLICATIONS: INCREASING ACCESS TO PROBLEM GAMBLING RESOURCES.**

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**Aims:** To demonstrate how web-based (including web accessible cell phone) technology can be used to enhance accessibility to problem gambling information and services. The need for this type of resource is supported by a 2008 web-based needs assessment conducted by the Mountain West Addiction Technology Transfer Center. The findings from that study, which examined substance abuse professionals' attitudes and level of interest in training and technical assistance, suggest that providers recognize the need to integrate technology enhancement applications in order to provide real-time certified data/information in a cost effective manner. Using a website developed in cooperation with the Nevada Council on Problem Gambling, a resource was created to facilitate access and dissemination of problem gambling resources. Resource development challenges included creating: 1) a website that automatically updated when a system user changed support or treatment location information; 2) a system that would quickly provide real-time information so the person in crisis could access the most current resources/services available without having to call anyone; and 3) the ability to generate PDFs that could be emailed to other agencies, thus cutting down time and costs.

**Conclusions:** Technology integration is an important factor in cutting costs related to redundant or time consuming tasks. Using the Resource Locator reduces costs by eliminating the need to send information through the mail or manually update a website with the most current information regarding treatment and support locations/attributes. When information is updated in the Resource Locator, it is immediately available to anyone searching for treatment or support services, regardless of the day or time. In addition, the types and locations of services for which people are searching are captured for statistical purposes, making it possible to improve service delivery.

**Support:** Funded by the Nevada Council on Problem Gambling

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**CHARACTERISTICS ASSOCIATED WITH SMOKING SEVERITY DURING PREGNANCY.**

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**Aims:** Identifying characteristics associated with severity of smoking during pregnancy may aid in establishing causality. In this study, we compared socioeconomic and other variables between pregnant women smoking at 3 different levels.

**Methods:** Pregnant women who reported being smokers when they learned of the current pregnancy (N=351) completed a battery of assessments at study intake and were divided into 3 groups: 1) those reporting smoking abstinence, which was biochemically-verified (urine cotinine (UC)  $\leq 80$ ng/ml), i.e., spontaneous quitters (n=118); 2) those reporting smoking (M=8.7 cigs/day) and with UC  $> 80$ ng/ml, i.e., cot (+) smokers (n=221); and 3) those reporting smoking (M=1.7 cigs/day) but with UC  $\leq 80$ ng/ml, i.e., cot (-) smokers (n=35).

**Results:** There was a main effect of group for 18/19 variables examined. Pairwise comparisons indicated that for 8 variables (age, education, age began smoking, withdrawal score, delay discounting rate, % married, % with private insurance, % with few friends/family who smoke, and % with depressive history), cot (-) smokers were more like cot (+) smokers. For 6 variables (# cigs/day pre-pregnancy, stress level, BDI score, % primigravida, % living with other smokers, and % with pre-pregnancy quit attempt), cot (-) smokers had values intermediate between cot (+) smokers and spontaneous quitters. For 2 variables (% employed and % who don't allow smoking in their home), cot (-) smokers were more like spontaneous quitters. For the # quit attempts during pregnancy, cot (-) smokers were different from both cot (+) smokers and spontaneous quitters.

**Conclusions:** Results suggest that cot (-) smokers have a number of characteristics like spontaneous quitters or intermediate between spontaneous quitters and cot (+) smokers; these may be variables that facilitate their substantial smoking reduction (~90%) during pregnancy. However, the large number of characteristics that cot (-) smokers share with cot (+) smokers may include variables that contribute to their inability to abstain completely.

**Support:** NIDA R01DA14028

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**RANDOMIZED, DOUBLE-BLIND TRIAL OF MODAFINIL VS PLACEBO FOR METHAMPHETAMINE DEPENDENCE.**

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**Aims:** Modafinil is a non-amphetamine stimulant that has shown promise as a treatment for cocaine dependence. We compared modafinil to placebo for reducing methamphetamine (MA) use and craving and increasing treatment retention among MA dependent participants.

**Methods:** Following a 2-week, non-medication baseline screening period, 71 treatment-seeking MA dependent participants were randomly assigned to modafinil (400mg daily) or placebo for 12-weeks under double-blind conditions. Participants attended clinic thrice weekly to provide urine samples analyzed for MA-metabolite, to complete research measures and assessments, and to receive contingency management and weekly cognitive behavioral therapy sessions.

**Results:** There were no statistically significant effects for modafinil relative to placebo on MA use verified by urine drug screens, for reducing MA-cravings, or on study retention.

**Conclusions:** Initial findings show modafinil was no more effective than placebo in reducing MA use, reducing cravings or improving retention. Studies in cocaine dependence suggest that 200mg daily may be more efficacious than the 400mg modafinil dose tested here. Further development of modafinil for MA dependence at the 400mg daily dose is not warranted.

**Support:** Funding for this study was provided by NIDA Grant 1 P50 DA 18185. Study medication and matching placebo tablets were supplied by Cephalon.

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**EFFECT OF NICOTINE ON ATTENTIONAL NETWORKS IN SMOKERS AND NONSMOKERS.**

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**Aims:** Research has identified three independent attentional networks involving alerting, orienting, and executive functions. Nicotine reliably enhances attention in smokers, but its effect in nonsmokers is not clear. We investigated the effect of nicotine on the efficiency of alerting, orienting, and executive attention in smokers and nonsmokers.

**Methods:** We tested 22 (of 30 planned) smokers and 20 (of 30 planned) nonsmokers at three sessions, separated by at least 24 hours. At each session, participants were administered a single dose of nicotine nasal spray (0, 0.5, or 1.5 mg). Testing with the Attention Network Test (ANT) began 5 minutes after dosing and lasted about 10 minutes. The ANT measures alerting, orienting, and executive attention using a combination of the cued reaction time and flanker tasks. Reaction time to targets was analyzed by analysis of variance using SPSS.

**Results:** There was a Group x Dose interaction ( $p = 0.03$ ) on alerting attention, such that the 0.5 mg nicotine dose improved alerting efficiency more in nonsmokers compared with smokers. Smokers showed greater executive attention efficiency than nonsmokers ( $p = 0.02$ ), but there was no effect of nicotine. Orienting attention did not differ as a function of group or nicotine dose.

**Conclusions:** Nicotine did not have a unitary effect on attention and produced different effects in smokers versus nonsmokers in alerting attention, suggesting that nicotine's effects on attention are more nuanced than previously thought. These results are consistent with the independence of attentional networks and may have implications for treating attentional difficulties observed during tobacco withdrawal.

**Support:** This research was supported by the Intramural Research Program of the NIH, National Institute on Drug Abuse.

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**COMPARATIVE NEUROCHEMICAL ANALYSIS OF ACCUMBENS AND VENTRAL TEGMENTUM DURING "SPEEDBALL," COCAINE AND HEROIN SELF-ADMINISTRATION.**

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**Aims:** A previous study from our lab demonstrated that intravenous self-administration of cocaine/heroin combinations (speedball) induces synergistic elevations in extracellular dopamine concentrations [DA]<sub>e</sub> in the nucleus accumbens (NAc) compared to cocaine and heroin alone. The aim of this study was to examine potential interaction s between extracellular concentrations of dopamine, serotonin, GABA and glutamate in the NAc and VTA during self-administration of cocaine, heroin and speedball combinations.

**Methods:** Male Fisher rats were trained to self-administer either cocaine (330, 165, 83 µg/inf), heroin (18, 9, 4.5 µg/inf) or cocaine/heroin combinations (330/18, 165/9, 83/4.5 µg/inf) under a multiple component self-administration sessions (1hr/component, descending dose order, FR2) for a minimum of 20 days prior to microdialysis. Samples were collected in 10 minute intervals from 30 minutes prior to 60 minutes following the self-administration session and analyzed using narrow bore RP-HPLC with electrochemical detection (DA and 5HT) and capillary electrophoresis with laser induced fluorescence (GABA and glutamate).

**Results:** Similar to our previous report, extracellular dopamine levels [DA]<sub>e</sub> were synergistically elevated in the NAc during speedball self-administration compared with cocaine and heroin alone. In the VTA, we found synergistic increases in [DA]<sub>e</sub> with speedball compared with cocaine and heroin alone. In the NAc and VTA, [5HT]<sub>e</sub> levels were slightly greater than cocaine alone and both were significantly greater than heroin alone. [Glu]<sub>e</sub> and [GABA]<sub>e</sub> in the NAc and VTA are currently being analyzed and will be presented at the meeting.

**Conclusions:** Defining the neurochemical and neuropharmacological indices using models of polydrug abuse is an essential step in the development of treatment strategies for the unique challenges posed by individuals with simultaneous addictions to multiple substances.

**Support:** R01DA012498 (SEH)

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**DEVELOPMENT OF COGNITIVE BEHAVIORAL THERAPY PLATFORM TARGETING BOTH COCAINE DEPENDENCE AND ADHD.**

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**Aims:** Cocaine dependence remains a significant problem, with limited treatment options. Treatment is especially problematic in individuals with comorbid psychiatric disorders. For example, individuals with attention-deficit hyperactivity disorder (ADHD) are at a greater risk for cocaine dependence, with a worse prognosis and more complicated pattern of remission and relapse. Moderate success has been demonstrated with cognitive behavioral therapy (CBT) platforms targeting cocaine use or ADHD in single-diagnosis populations, however no protocol uniquely targets comorbid cocaine dependence and ADHD. Thus, we developed a manual-driven CBT platform for this dual diagnosis population based on a CBT protocol previously employed by our group. The aim of the manual was to integrate strategies for treatment of this comorbidity during weekly sessions, with emphasis on the interplay between cocaine dependence and ADHD.

**Methods:** The first two modules included introductory information about the program and cocaine dependence, followed by ADHD psychoeducation. The use of a calendar/notebook system was also introduced and used throughout the program. Subsequently, four core sessions covered overlapping symptomatology between ADHD and cocaine dependence, and addressed appropriate coping strategies. Eight elective sessions were also included to individualize treatment. These sessions covered topics such as assertiveness, anger management, impulsivity, and procrastination.

**Results:** This protocol was implemented in a 12-week pilot study investigating the utility of CBT plus sustained release d-amphetamine to treat comorbid cocaine dependence and ADHD. The dual-focused CBT procedure was well-received by patients, and case reports will be discussed.

**Conclusions:** Collectively, these data suggest potential utility for a modified CBT procedure targeting cocaine dependence and ADHD simultaneously.

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**SMOKING OPINIONS AND ATTITUDES AMONG PREGNANT SMOKERS AND SPONTANEOUS QUITTERS.**

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**Aims:** Eighteen percent of women in the US are current cigarette smokers. Some (20%) quit with little or no intervention upon learning they are pregnant (i.e., spontaneous quitters), but the majority will continue to smoke. Prior reports have indicated that, compared to continuing smokers, spontaneous quitters perceive greater risk of harm to the fetus as a result of smoking (e.g., Ockene et al., 2000). The aim of the present ongoing study was to more fully characterize smoking opinions and attitudes among these two groups using a more comprehensive instrument.

**Methods:** Participants were pregnant smokers (n=126) and spontaneous quitters (n=34) enrolled in ongoing randomized controlled trials to promote smoking cessation and relapse prevention during pregnancy and postpartum. At trial intake, all participants completed a 23-item, Likert-scale questionnaire on smoking opinions and attitudes adapted from Johansson et al. (2004). Participants indicated their level of agreement with statements about smoking in general, smoking during pregnancy, smoking postpartum, and the dangers of second-hand smoke.

**Results:** Spontaneous quitters reported that they would be more ashamed than smokers to tell their OB that they smoke ( $p < .05$ ). Spontaneous quitters also disagreed more strongly with the statement that smoking postpartum is ok as long as it is done outdoors ( $p < .01$ ). Three additional statements regarding smoking in general suggested that spontaneous quitters had less smoking-friendly opinions and attitudes, but these did not reach conventional levels of statistical significance at this time.

**Conclusions:** These results suggest that spontaneous quitters differ from continuing smokers in regard to some smoking opinions and attitudes. These differences may suggest areas for targeting further efforts to inform pregnant and postpartum women about the risks of smoking during and after pregnancy.

**Support:** NIDA R01DA14028 and T32DA07242

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**TRANSDERMAL BUPRENORPHINE TO SWITCH PATIENTS FROM HIGHER-DOSE METHADONE TO BUPRENORPHINE WITHOUT SEVERE WITHDRAWAL SYMPTOMS.**

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**Aims:** Prolonged QTc-intervals and other conditions may necessitate switching patients in methadone maintenance treatment (MMT) to buprenorphine. This procedure can cause serious withdrawal symptoms if methadone doses are higher than 30mg per day and/or if patients do not wait long enough. This study evaluated whether buprenorphine patches would be helpful in blunting withdrawal symptoms if patients on higher doses of methadone (60-100mg) must be switched to buprenorphine.

**Methods:** Eleven heroin dependent patients in MMT (mean methadone dose: 70 mg, range: 60 to 100mg) were admitted to the Psychiatric University Hospital for five days. A buprenorphine patch (35 µg, Transtec®) was attached 12 hours after last methadone intake. Forty-eight and 60 hours later, patients were treated with 2mg of sublingual buprenorphine (Subutex®). Oral buprenorphine was increased from 4mg to 24mg per day during the following three days and then titrated clinically. Blood and urine samples were collected prior to patch application. ECG and vital signs were done on admission or during the whole inpatient period. Severity of withdrawal was self-reported every day, using the Short Opiate Withdrawal Scale. The Beck Depression Inventory and the Beck Anxiety Inventory were administered on day one and 60 of the study. Follow-up visits were at day nine and 60 post discharge, including ECGs and urinalyses.

**Results:** Ten patients were successfully switched from methadone to buprenorphine. Withdrawal symptoms were rated as "mild" or "nonexistent" by five. BDI-V and BAI-scores decreased to follow up, indicating greater satisfaction with buprenorphine.

**Conclusions:** This pilot study suggests that transdermal buprenorphine might be efficacious in blunting withdrawal symptoms in patients on higher methadone doses. Thus, this new procedure might better be able to retain patients who might have left substitution treatment due to adversities of former switching protocols.

**Support:** This work did not receive any financial support

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**CHANGES IN MGLUR5 SURFACE EXPRESSION: COMPARISON BETWEEN REPEATED MORPHINE AND METHAMPHETAMINE.**

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**Aims:** Glutamate transmission, including activation of metabotropic and ionotropic receptors, is key to behavioral sensitization, the progressive increase in motor activity after repeated drug treatment. The metabotropic glutamate receptor group I, subtype 5 (mGluR5) modulates neuroplasticity associated with sensitization to both opiates and stimulants. For example, mGluR5 antagonists block the expression of morphine-induced motor sensitization (Kotlinska & Bochenski 2007) and decrease the acute hyperlocomotion induced by stimulants (McGeehan et al. 2004). Expression levels of mGluR5 are high in the medial prefrontal cortex (mPFC), nucleus accumbens (NAc), and ventral pallidum (VP), all key anatomical substrates of behavioral sensitization. Levels of mGluR5 are decreased in the NAc after 1 and 3 weeks withdrawal from sensitizing treatment regimens of cocaine (Mao & Wang 2001, Swanson et al. 2001). The aim of the current study was to determine if withdrawal from repeated treatment with morphine (Morph) or methamphetamine (Meth) alters surface expression of mGluR5 in the afore-listed brain regions.

**Methods:** Rats were treated with saline (1ml/kg), Morph (8mg/kg), or Meth (1mg/kg) once a day for three days. Motor sensitization developed in the Morph and Meth-treated groups. Rats were sacrificed after 14 days of withdrawal. The mPFC, NAc and VP were dissected, processed for mGluR5 cross-linking and assayed by immunoblotting according to method of Budreau and Wolf (2005).

**Results:** Repeated Meth treatment increased the mGluR5 surface/intracellular (S/I) ratio in the VP compared to rats treated with saline ( $p < 0.05$ ). In contrast, repeated Morph treatment increased the mGluR5 S/I ratio in the mPFC ( $p < 0.05$ ).

**Conclusions:** Thus, mGluR5 trafficking is differentially altered by withdrawal after repeated treatment of two different classes of abused drugs.

**Support:** This study was supported by USPHGs DA023306 to AAH and TCN and DA015760 to TCN.

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**SMOKING CESSATION AND BREASTFEEDING.**

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**Aims:** This study examined whether smoking-cessation affected breastfeeding during the initial 6 months postpartum. Study participants received smoking-cessation therapy across three randomized clinical trials examining whether abstinence-contingent vouchers increased smoking abstinence.

**Methods:** Study participants (n = 153) were randomized to Contingent or Noncontingent Voucher conditions. In the Contingent condition, participants earned incentives contingent on smoking abstinence from the start of prenatal care through 3-months postpartum. In the Noncontingent condition, participants received vouchers independent of smoking status. Smoking status was assessed throughout antepartum and at weeks 2, 4, 8, 12, and 24 postpartum. Breastfeeding outcomes were evaluated using self-report at each of the postpartum assessments. Treatment comparisons were conducted using chi square tests.

**Results:** As reported previously, smoking abstinence was greater in the Contingent than the Noncontingent conditions antepartum and through 12-weeks postpartum, although not at 24-weeks postpartum after incentives were discontinued. There was no treatment effect on initiation of breastfeeding, with 56% vs. 49% and 48% vs. 39% of women in the Contingent and Noncontingent conditions reporting breastfeeding at 2 and 4-weeks postpartum. However, there was a treatment effect on the duration of breastfeeding, with 40% vs. 25% and 35% vs. 17% of women in the Contingent vs. Noncontingent conditions breastfeeding at the 8- and 12-week assessments ( $p < .05$ ). A non-significant trend remained evident at the 24-week assessment, with rates being 20% and 13% in the Contingent and Noncontingent conditions. Breastfeeding duration covaried with the differential prevalence of postpartum smoking abstinence.

**Conclusions:** Abstinence-contingent vouchers increase the duration of breastfeeding by increasing postpartum smoking abstinence. These effects on breastfeeding document a previously unrecognized health benefit to the newborn of maternal smoking cessation and provide a substantive rationale for continuing abstinence-contingent vouchers beyond 12-weeks postpartum.

**Support:** R01 DA14028 from NIDA

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### THE IMPACT OF SOCIAL AND EMOTIONAL ISOLATION ON RISKY BEHAVIORS AMONG WOMEN INJECTION DRUG USERS IN PORTLAND, OR.

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**Aims:** Field a survey instrument to measure demographic characteristics, drug use history, social/emotional isolation and engagement in risky behaviors among women injection drug users (IDUs). Examine data for an association between isolation and engagement in risky behaviors.

**Methods:** This study employed a cross sectional design, collected data from 102 women IDUs through a self report questionnaire on social/emotional isolation and engagement in HIV/HCV risk behaviors. All subjects were adult women of any race/nationality who spoke English and who, by self report, had injected drugs at least one time over the past 30 days.

**Results:** Descriptive statistics: 73.5% were white with an average age of 34, 55.9% were homeless, 82.4% unemployed, 31.4% in treatment, and 56% injected at least once per day. 55% used cocaine, 75% heroin, 48% heroin and cocaine together and 53% amphetamines. 67% were both emotionally and socially isolated. Risk behaviors included: injecting with used equipment (43%), injected by another (40%), sex with two or more partners (32%), sex with IDU (30%), exchanging sex for money or drugs (29%), and not always using condom when exchanging sex for money or drugs (87%). Preliminary analysis revealed positive associations between isolation and two risk behaviors (sharing injection equipment and trading sex for money or drugs)  $p = .006$  and  $.02$ .

**Conclusions:** Women IDUs are at increased risk for infection with blood borne and sexually transmitted diseases. Investigators have found that the character and dynamic of social interactions are important determinants of risk. Social and emotional isolation are facets of social interactions that have not been widely considered with respect to HIV or HCV risk. Data from this research documents high levels of isolation among women IDUs. Preliminary analysis highlights possible associations between isolation and engagement in risk behaviors. This provides insight allowing researchers to plan interventions that address issues of isolation to combat the spread of HIV and HCV.

**Support:** Awards from the OHSU Tarter Trust and the Mitch Greenlick Foundation supported this research.

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### USING RESPONDENT DRIVEN SAMPLING TO ENHANCE RECRUITMENT OF DUALY-DIAGNOSED ADOLESCENT CLINICAL TRIAL PARTICIPANTS.

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**Aims:** A lack of research on effective methods of recruiting dually-diagnosed adolescents to clinical trials has been a barrier to addressing research gaps in this important clinical population. We report on the use of respondent driven sampling (Heckathorn, 1997) to enhance recruitment efforts at one of eleven community-based substance treatment programs participating in a Randomized Controlled Trial of Osmotic-Release Methylphenidate (OROS-MPH) for Attention Deficit Hyperactivity Disorder (ADHD) in adolescents with Substance Use Disorders (SUD) conducted in the National Drug Abuse Treatment Clinical Trials Network (CTN). Site recruitment efforts initially focused on evaluating adolescents meeting pre-screening criteria who were referred to the treatment program Lexington-Richland Alcohol and Drug Abuse Council (LRADAC) through existing referral sources (e.g. juvenile justice, social services, schools). Slower than expected recruitment prompted study staff to request IRB approval to compensate study participants who referred potential study participants from among their acquaintances who successfully completed the informed consent process. The compensation amount was \$10.

**Results:** Thirty-two adolescents (ages 13-18) were enrolled at the LRADAC site. Nineteen of the adolescents enrolled in the study were recruited from existing treatment program referral sources. Recruitment efforts were significantly enhanced by RDS after IRB approval at approximately study mid-point. Thirteen of the thirty-two participants enrolled at the LRADAC site were recruited from referrals by other study participants (RDS).

**Conclusions:** Respondent driven sampling may be an effective method to enhance recruitment of dually-diagnosed adolescents for clinical trial participation.

**Support:** National Drug Abuse Treatment Clinical Trials Network (CTN)

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### VARIATION IN RETENTION BY BEHAVIORAL CONDITION IN BUPRENORPHINE TREATMENT FOR OPIOID DEPENDENCE.

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**Aims:** Physicians in the U.S. are required to include a psychosocial treatment component when prescribing buprenorphine for opioid dependence. Some may provide this component in a medical management format while others may offer referrals to local psychosocial treatment programs.

**Methods:** In an ongoing NIDA-funded trial, opioid-dependent individuals presenting for treatment are provided with a platform of buprenorphine pharmacotherapy and, after a 2-week induction/stabilization period, are randomly assigned to 1 of 4 psychosocial treatment conditions (cognitive behavioral treatment [CBT]; contingency management [CM]; combined CBT and CM [CBT+CM]; and medical management [MM]). The current study reports on preliminary findings from data collected from the first 60 participants during the psychosocial treatment phase (weeks 3-18) to determine whether there are differences in retention by psychosocial condition. Retention is measured dichotomously as completion of the psychosocial treatment phase, and numerically as the last clinic visit.

**Results:** Results indicate no differences in baseline characteristics between study conditions. The percentages of participants in each condition completing the 18-week psychosocial treatment phase are: CBT = 78.6%; CM = 75.0%; CBT+CM = 66.7%; and MM = 53.3%. Mean last visit number is 16.6 (3.8) for the CBT group, 16.4 (3.6) for the CM group, 15.5 (4.5) for the CBT+CM group, and 14.5 (4.7) for the MM group. Because the CM condition offers incentives for combined attendance and urine results, analyses examined whether this condition would experience a fewer number of missed clinic visits. Results show that the CM group did not attend a greater number of clinic visits despite incentives.

**Conclusions:** The benefits of adding a psychosocial treatment component to treatment with buprenorphine are discussed.

**Support:** NIDA Grant DA020210

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### THE EFFECTS OF ALLOPREGNANOLONE ON COCAINE SELF-ADMINISTRATION UNDER A PROGRESSIVE RATIO SCHEDULE IN FEMALE RATS.

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**Aims:** Sex differences have been found in the subjective effects of cocaine and cocaine-related behavior. Females in the luteal phase of their menstrual cycle show diminished subjective cocaine effects compared to women in the follicular phase. Clinical and preclinical research suggests that such differences are due to gonadal hormones. For example, progesterone (PROG) suppresses the escalation of self-administered cocaine during periods of extended access in female rats. Such actions of PROG may be due in part to a PROG metabolite, allopregnanolone (ALLO). ALLO is a potent allosteric GABBA-A modulator that, like PROG, has been shown to decrease the reinstatement of cocaine-seeking activity in female rats. Thus, the present study examined the effects of ALLO on the maintenance of cocaine self-administration using a progressive ratio schedule.

**Methods:** Female rats were trained to administer cocaine (0.4 mg/kg/infusion, i.v.) under a fixed ratio (FR1) schedule until criteria for stability were met (> 30 infusions cocaine for 3 days). Next, rats were given randomly selected doses of cocaine (0.2, 0.4, 0.8, or 1.6 mg/kg), to obtain a dose-response function. During this phase, vehicle (VEH, peanut oil, s.c.) was administered 30 min prior to each 2 2-hr daily session. Next, dose-response curves were again established for all cocaine doses (0.2, 0.4, 0.8, or 1.6 mg/kg, randomly selected), and ALLO (15 or 30 mg/kg) was administered 30 min prior to session instead of VEH.

**Results:** Compared to VEH, rats achieved fewer mean infusions of the 0.2 mg/kg dose when administered ALLO (15 and 30 mg/kg).

**Conclusions:** These results suggest that ALLO reduces the motivation of female rats to administer the 0.2 mg/kg dose of cocaine, and further supports ALLO's potential as a novel therapy for cocaine dependence amongst female abusers.

**Support:** Supported by R01 DA003240-24, K05 DA015267-07 (MEC).

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**FACTORS ASSOCIATED WITH NONMEDICAL USE OF PRESCRIPTION DRUGS.**

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**Aims:** Understanding factors related to the nonmedical use of prescription drugs (i.e., using prescription drugs without a doctor's order or using in a way other than prescribed) is important for prevention and intervention efforts. The objective of this work was to identify individual, partner, and relationship factors that were associated with nonmedical use of prescription drugs.

**Methods:** Couples (N = 371) prescription drug use, alcohol use, psychological functioning, relationship factors, and sociodemographic factors smoking were assessed at the time they applied for their marriage license and then again at the first, second, fourth, seventh, and now ninth anniversaries. For this report, we focus exclusively on the last assessment.

**Results:** At the last assessment, 7.3% of husbands and 13.5% of wives reported nonmedical use of prescription drugs. Among husbands, we did not identify any factors related to an increased likelihood of prescription drug use. Among wives, however, a variety of individual, partner, and relationship factors were associated with nonmedical use. Wives with higher levels of depression and lower levels of marital satisfaction were more likely to use prescription drugs in a nonmedical fashion. Although wives' frequency of heavy drinking was not associated with nonmedical drug use their husbands' heavy drinking was associated with wives' nonmedical use of drugs. Further, wives were more likely to use drugs non-medically when married to husbands who used prescription drugs (as prescribed or non-medically).

**Conclusions:** When husbands' prescription drug use was separated into non-medical use and medical use, only medical use of prescription drugs was associated with wives' nonmedical use. Thus, it appears that access, rather than pattern of use, of a spouse was associated with nonmedical use in wives.

**Support:** Supported by NIAAA grant R37-AA009922 awarded to KEL

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**ASSESSMENT OF EFFORT ON NEUROPSYCHOLOGICAL TESTING IN DRUG ABUSE RESEARCH.**

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**Aims:** AIM: Many research studies in drug abuse research use neuropsychological testing to assess brain damage. Recent concerns have been raised concerning the possibility that poor effort by research subjects may produce poor scores on neuropsychological testing and thereby produce spurious results in drug abuse research. This poster addresses this issue by examining the relationship of poor effort to a neuropsychological test frequently used in drug abuse research-Trail Making Test (TMT) - and illustrates how this relationship can be used to determine if poor effort has influenced drug abuse research results.

**Methods:** METHOD: Data on results with the TMT in samples that were determined to demonstrate good effort and poor effort will be reviewed. Expectations for levels of performance associated with good effort will be estimated.

The relationship of neuropsychological testing in a drug abuse research sample with poor effort will be illustrated using a sample of 5619 males and 2902 females.

**Conclusions:** CONCLUSION: Levels of performance on neuropsychological testing can be used to estimate if poor effort has produced spurious results.

**Support:** Supported by private funds only

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**DEVELOPMENT OF INJECTION HIV RISK BEHAVIORS IN ADOLESCENTS FOLLOWED INTO YOUNG ADULTHOOD.**

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**Aims:** To examine predictors of injection drug use and risky sexual behavior in a sample of adolescents followed into young adulthood

**Methods:** 2634 adolescents were followed longitudinally five years after initial assessment. The sample consisted of a general population twin sample (N= 2332) as well as sample of youth ascertained from substance abuse treatment and their siblings (N=302). Descriptive statistics and predictors of Wave II injection drug use and risky sexual behavior status were analyzed.

**Results:** 41 subjects reported injection drug use at five year follow-up. The best predictors of wave 2 injection drug use were age of initiation of drug use and total number of drugs used at wave 1. . Risky sex at wave 2 was significantly predicted by wave 1- number of cannabis symptoms and wave 1 – number of conduct disorder symptoms.

**Conclusions:** Development of HIV related risk behavior in a longitudinal sample of adolescents followed into young adulthood was differentially predicted, with Injection drug use being predicted by early age of initiation into drug use as well as the total number of drugs used during adolescence, whereas risky sexual behavior was predicted by the number of conduct disorder symptoms and severity of involvement with cannabis use.

**Support:** DA015522, DA011015

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**ENHANCED BRAIN METABOLIC EFFECTS OF ACUTE COCAINE ADMINISTRATION FOLLOWING AN EXTENDED PERIOD OF COCAINE SELF-ADMINISTRATION IN NONHUMAN PRIMATES.**

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**Aims:** Functional neuroimaging studies have documented cocaine-induced brain metabolic effects in humans that may play an important role in the etiology of drug addiction. The present study employed a within-subjects design in nonhuman primates to establish the influence of drug history on the acute brain metabolic effects of cocaine.

**Methods:** Experimentally naïve rhesus monkeys (N=6) were trained to self-administer cocaine (0.1mg/kg/injection) under a fixed-ratio 20 response (FR20) schedule of i.v. drug delivery. Over a 10-week period of limited access, subjects could receive a total of 10 injections during daily, 1-hour sessions. Subsequently, over a 10-week period of extended access, subjects could receive a total of 60 injections during daily 4-hour sessions. The acute brain metabolic effects of cocaine were determined with PET neuroimaging and flurodeoxyglucose (FDG) in drug naïve subjects, and following the limited-access and extended-access conditions. FDG (15 mCi) was administered i.m. in the home cage and either cocaine or saline was administered i.m. 5 minutes later. Following a 45-minute FDG uptake phase, subjects were anesthetized and transported to a MicroPET 220 focus scanner for image acquisition. The corresponding t-maps documented significant regional differences in FDG uptake between cocaine and saline conditions.

**Results:** In drug naïve subjects, cocaine induced robust increases in brain metabolism in prefrontal regions, consistent with effects on cerebral blood flow reported previously in rhesus monkeys. Importantly, the effects were more robust and extensive following a progressive history of cocaine self-administration.

**Conclusions:** The longitudinal design employed in nonhuman primates offers distinct advantages toward understanding relevant neurobiological changes associated with escalated cocaine use.

**Support:** Supported by USPHS Grants DA00517 (LLH), DA10344 (LLH) and RR00165.

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**LIFE COURSE TRAJECTORIES OF EMPLOYMENT: EXPLORING THE IMPACTS OF DRUG USE.**

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**Aims:** To identify patterns of employment trajectories over time and to examine these employment patterns in relation to drug use.

**Methods:** Data are based on 7,661 individuals (3,677 males and 3,984 females) who participated in the 1979 National Longitudinal Survey of Youth (NLSY79). Bivariate random intercept and slope modeling (RISM) was applied to examine the relationship between employment trajectory and marijuana-use trajectory from age 23 to age 39 and growth mixture modeling (GMM) was applied to identify distinctive employment trajectory groups for each gender.

**Results:** Lifetime marijuana use is 82% for males and 69% for females. RISM showed that at age 23, employment and marijuana use is negatively correlated ( $-0.05$  for males and  $-0.06$  for females) indicating marijuana use may decrease employment. For both gender, the employment slope is positively correlated with employment intercept ( $r=0.20$  for males and  $r=0.23$  for females), indicating employment at age 23 has a positive impact on subsequent employment trajectory. Only for males the employment slope is negatively correlated with marijuana intercept ( $r=-0.07$ ), indicating marijuana use may decrease employment over age. For both gender, marijuana slope is not significantly correlated with employment slope. GMM identified 5 distinct groups for men and women. For males, 76.5% is in the High group, 6.2% in the Decreased group, 7.9% in the Increased-early group, 4.2% in the Increased-late group and about 5% in the Low group. For females, a U-shape trajectory is identified for 7.9% of females, in addition to the High (58.8%), Decreased (7.3%), Increased-early (13.2%), and Increased-late (12.8%) groups. Subjects with distinctive trajectories of employment significantly differ on ethnicity and drug use, with marijuana use lower in High and Increased-early groups for both gender.

**Conclusions:** Marijuana use has negative impact on employment trajectories, and the relationships are stronger among men.

**Support:** P30 DA016383 & K05DA017648 from the National Institute on Drug Abuse.

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**ALCOHOL ABUSE AND DEPENDENCE CRITERIA AMONG STUDENTS AT TWO SCHOOLS IN PUERTO RICO: A LATENT CLASS ANALYSIS.**

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**Aims:** Although the Diagnostic and Statistical Manual of Mental Disorders (DSM), Fifth Edition is scheduled to be completed in the next few years, there is still question about the validity of a diagnosis of Alcohol Abuse or Dependence among youths, especially youths from an ethnic minority. This study will examine the co-occurrence of Alcohol Use Disorder criteria among Puerto Rican youths by classifying adolescents into latent classes based on their observed patterns of Alcohol Abuse and Dependence criteria endorsement.

**Methods:** This study will use cross-sectional data collected in 2000 from the International Longitudinal Survey of Adolescent Health administered to 972 youths attending one middle school or one high school in San Juan, Puerto Rico. Youths were 11-19 years of age and 57% were female. Latent class analysis was used to classify youths according to their pattern of endorsement of four Alcohol Abuse criteria and six Alcohol Dependence criteria.

**Results:** This study found that a two class model appropriately fit the data (Entropy=0.96). The first class (N=89, 9.2%) had a high prevalence of Alcohol Abuse and Dependence criteria while the second class (N=883, 90.8%) had a low prevalence of Alcohol Abuse and Dependence criteria.

**Conclusions:** The pattern of endorsement of Alcohol Abuse and Dependence criteria did not support the current DSM diagnostic distinction between Alcohol Abuse and Dependence among Puerto Rican youths, as many youths in the first class endorsed both Abuse and Dependence criteria

**Support:** This research was supported by NIDA Grants DA00254 and DA007292.

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**DEVELOPMENTAL TRAJECTORIES OF HIV SEXUAL RISK BEHAVIORS FROM ADOLESCENCE TO YOUNG ADULTHOOD.**

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**Aims:** This study identifies distinctive gendered trajectories of HIV sexual risk behaviors and examines how the trajectories are influenced by drug use, delinquency, and other factors.

**Methods:** Using group-based trajectory modeling on sexual risk score derived from: number of sexual partners, times of sexual intercourse, and frequency of condom use, from ages 15 to 23, this study uses data from the 1997 National Longitudinal Survey of Youth (NLSY97) to examine the trajectories of sexual risk among 5,419 adolescents (2,798 males and 2,621 females) who were 12 to 14 years old on December 31, 1996.

**Results:** Five distinctive gendered trajectory groups (High, Decreased, Increased-early, Increased-late, and Low) were identified. For males, 20.1% were in the High group with a risk trajectory that was high at age 15 and increased over the observed ages. The risk trajectory for the Decreased group (18.2%) was high before age 19, but decreased afterwards. The risk trajectories of the Increased-early and Increased-late groups (24.7% and 19.9%, respectively) were low at age 15, but increased significantly starting at age 16 for the former group and at age 18 for the latter group. About 17% of males remained at low risk over the observation period. For females, the risk trajectory groups were: High (18.6%), Decreased (9.8%), Increased-early (31.7%), Increased-late (22.8%), and Low (17.1%). Alcohol use, marijuana use, and engagement in delinquent behaviors by age 16 were significantly different among adolescents in distinctive trajectory groups. For both genders, adolescents in the High group had the highest days of alcohol or marijuana use per month and were more likely to engage in delinquent behaviors. Our findings also identified the following potential risk/protective factors: ethnicity, parental support, dating by age 12, having sex by age 14, and marital status.

**Conclusions:** Sexual-risk trajectories are heterogeneous among adolescents and significantly correlate with alcohol/drug use and delinquency.

**Support:** 1R03MH084434-01A1 from the National Institute of Health

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**A STUDY OF SUBSTANCE ABUSE IN THE ASIAN INDIAN COMMUNITY IN ONTARIO, CANADA.**

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**Aims:** To find out the type of substances abused and the psychosociodemographic particulars about the substance abusers in Asian Indian population in Ontario, Canada.

**Methods:** 30 cases of substance abuse were studied. The cases were primarily obtained from the Asian Indian community in Ontario, Canada by the snowballing method. A specially designed proforma was used to obtain the psychosociodemographic particulars and the data regarding drug use and the effects of their use. ASI (Addiction Severity Index) was used to assess the severity of the substance abuse, and to study about the patterns of substance abuse. Psychiatric examination was done for all patients. DSM IV Diagnostic Criteria were used for diagnosis of substance abuse and for psychiatric diagnosis. The data will be analysed for descriptive statistics using SPSS.

**Results:** Preliminary results available include alcohol being the most common substance of abuse, followed by poppy flower in this population. The age ranged from 16 years to 63 years, the abusers were predominantly male and most were involved in labour work. Many of them had marital and relationship problems, history of domestic violence, legal problems connected to impaired driving and domestic violence, work problems, physical and mental health problems.

**Conclusions:** Preliminary results available indicate fairly severe substance abuse problems in the Asian Indian community in Ontario, Canada and other family, social, occupational and legal problems related to alcohol and drug use.

**Support:** The support from the data from the studies indicate fairly severe substance abuse problems in the Asian Indian community in Ontario, Canada and other family, social, occupational and legal problems related to alcohol and drug use.

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**EXPOSURE TO ALCOHOL DURING ADOLESCENCE OR ADULTHOOD ALTERS THE AVERSIVE AND LOCOMOTOR-ACTIVATING EFFECTS OF COCAINE IN ADULT RATS.**

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**Aims:** Although alcohol exposure during adolescence produces lasting behavioral and neural changes, little work assesses if such exposure impacts the response to other drugs taken later in life. Accordingly, in the present studies the effects of adolescent (and adult) alcohol exposure on the aversive and locomotor-activating effects of cocaine were studied.

**Methods:** Male Sprague Dawley rats were exposed to alcohol or vehicle for 10 days (Exp. 1: PND 30-39; Exp. 2: PND 70-79; 2 mg/kg). Taste aversion conditioning began on PND 65 (Exp. 1) or PND 105 (Exp. 2). During conditioning, subjects were presented with a novel saccharin solution followed by IP injections of cocaine (32 mg/kg) or saline given 15, 180 or 300 min after saccharin access. Following each injection, animals were placed in locomotor chambers where activity levels were measured for 1 h.

**Results:** Exp. 1: Animals exposed to vehicle during adolescence avoided the cocaine-associated solution with the degree of the aversion inversely associated with the delay. Animals exposed to ethanol showed a decrease in consumption only at the 15- and 180-min delays. Alcohol-exposed animals displayed weaker aversions than vehicle-preexposed animals. Groups preexposed to alcohol showed a decrease in gross and an increase in fine motor activity in response to cocaine (relative to controls).

Exp. 2: Animals preexposed to vehicle as adults avoided the cocaine-associated solution with the degree of the aversion inversely associated with the delay. Animals preexposed to alcohol showed a consistent decrease in consumption only at the 15-min delay. Groups preexposed to alcohol displayed weaker aversions than vehicle-preexposed animals. There was no effect of preexposure for either gross or fine motor activity.

**Conclusions:** Exposure to alcohol (adolescents or adults) attenuated the aversive effects of cocaine. The locomotor-activating effects of cocaine were only altered following adolescent preexposure. These results suggest that exposure to alcohol, whether during adolescence or adulthood, may alter the abuse liability of cocaine.

**Support:** Mellon Foundation (ALR)

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**DEPRESSION AND IMPULSIVITY IN ADOLESCENT SMOKERS AND NONSMOKERS.**

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**Aims:** Delay Discounting is an index of impulsive choice, and numerous studies have shown that addicted participants discount more by delay (i.e., perform more impulsively) than never-addicted control participants (see Reynolds, 2006, for review). However, little research has explored the relationship between delay discounting and depression.

**Methods:** The current study examined discounting and depression (Beck Depression Inventory II, BDI-II) in adolescent smokers (n = 20) and nonsmokers (n = 20). For comparison purposes a self report measure of impulsivity also was included (Barratt Impulsiveness Scale- Adolescent, BIS 11-A).

**Results:** Daily smokers had significantly higher cotinine levels (a metabolite of nicotine) than nonsmokers, thus verifying cigarette smoking status. However, the smokers and nonsmokers did not differ on measured demographic variables, e.g., age, race, household income, intelligence quotient. The smokers discounted more by delay [F(1, 38) = 5.76, p = .011], rated themselves as more impulsive on the BIS-11-A [F(1, 38) = 5.19, p = .014], and were more depressed [F(1, 38) = 3.27, p = .04] than the nonsmokers. To explore these data further, correlations between these three variables were evaluated. The measure of delay discounting and the BIS-II-A were not significantly correlated (p > .05). However, the BIS-11-A and the BDI-II were significantly correlated [r(39) = .424, p = .006]. Also, a multivariate logistic regression analysis indicated that neither the BIS-11-A nor BDI-II were significant independent predictors of smoking status; however, the measure of delay discounting still accounted for significant unique variance in smoking status beyond what was accounted for by self reported impulsivity and depression.

**Conclusions:** These findings indicate that delay discounting and self reported impulsivity relate differently to depression in adolescents, and further, that delay discounting is associated with adolescent cigarette smoking status differently than self reported impulsivity or depression.

**Support:** Two research grants from the College of Social and Behavioral Sciences, The Ohio State University (no i.d. number)

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**SOCIAL SUPPORT MODERATES BIOLOGICAL AND SUBJECTIVE RESPONSES TO STRESS AND DRUG CUES IN COCAINE-DEPENDENT INPATIENTS.**S M Hyman<sup>1</sup>, H Fox<sup>1</sup>, M J Kreek<sup>2</sup>, R Sinha<sup>1</sup>; <sup>1</sup>Psychiatry, Yale University School of Medicine, New Haven, CT, <sup>2</sup>Laboratory on the Biology of Addictive Diseases, Rockefeller University, New York, NY

**Aims:** BACKGROUND: Social Support is known to protect against stress and substance use relapse. AIM: To examine subjective (craving, anxiety) and biological (cortisol, ACTH) responses to stress and drug-cue exposure in cocaine dependent treatment-engaged individuals with high and low levels of social support.

**Methods:** METHOD: Cocaine dependent men and women engaged in inpatient treatment were divided into high (n = 30) and low (n = 31) social support groups based on responses to the Interpersonal Support Evaluation List (ISEL). All patients participated in a 3-day laboratory experiment in which they were exposed to personalized stress, drug-cue, and neutral/relaxing imagery. Subjective (craving, anxiety) and blood assessments (cortisol, ACTH) were taken prior to and immediately following imagery and at various recovery time-points.

**Results:** RESULTS: There were no basal differences on any of the measures. There was a group x condition effect for cocaine craving (p < .04) cortisol (p = .002) and ACTH (p = .008) and a group X condition X time-point interaction for Anxiety (p = .05). Specifically, subjects low in perceived social support demonstrated higher cocaine craving, cortisol, and ACTH following exposure to stress and drug cues compared with subjects high in perceived social support. Also, subjects low in social support reported greater overall anxiety across all 3 conditions compared with those high in social support (p = .01). Their anxiety ratings also took longer to return to baseline following exposure to stress and drug cues.

**Conclusions:** CONCLUSION: As increases in stress-induced craving and HPA axis markers are associated with relapse to cocaine, social support may represent a salient factor relating to treatment outcomes in this population.

**Support:** This research was supported by NIH grants P50-DA16556 (RS), K02-DA17232(RS), and P60-DA05130 (MJK).

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**AN OBJECTIVE QUANTITATIVE METHOD OF MONITORING ILLICIT DRUG USE.**Rodney J Irvine<sup>1</sup>, C Kostakis<sup>2</sup>, P Felgate<sup>2</sup>, J M White<sup>1</sup>; <sup>1</sup>Pharmacology, University of Adelaide, Adelaide, SA, Australia, <sup>2</sup>Forensic Sciences, Department of Justice, Adelaide, SA, Australia

**Aims:** The major method for determining the amount of illicit drug use in most communities is through self-report surveys. This relies on people accurately reporting their own drug use, but it is known that alcohol consumption is significantly under-estimated using this method. In the case of illicit drugs we would expect the degree of under-reporting to be at least as great, but currently there is no objective measure. Recent studies suggest that chemical analysis of sewage may be a means of providing an objective and accurate method for estimating rates of use of illicit drugs. The aim of the present study was to compare rates of drug use in the Australian community based on this method to rates determined from self-report and other sources.

**Methods:** Calculations of drug exposure per 1000 of the population were based on concentration of drug measured in sewage (determined by LC-MS), daily flow rates and population served by the sewage plant. Samples were collected weekly and tested for the presence of morphine, methamphetamine and MDMA.

**Results:** The results from the initial sample showed the presence of each of the drugs: morphine (1.1 µg/L), methamphetamine (5.5 µg/L) and MDMA (0.38 µg/L). The methamphetamine and MDMA concentrations are well above those reported in Europe and this is consistent with Australia's high rates of consumption of these drugs. The concentration of MDMA together with survey information suggests that 15 MDMA pills were consumed per 1000 of the population per day. Further data will be presented.

**Conclusions:** Analysis of sewage represents a novel approach to objectively measuring population drug use. The results to date show that international comparisons of amounts of use can be made that are independent of the various influences on self-report. Further data will show the potential to monitor repeatedly in order to detect changes in drug use over both long and short time courses.

**Support:** University of Adelaide

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**GENDER DIFFERENCES IN PHYSICAL/SEXUAL ABUSE IN OUTPATIENTS WITH SUDS: CORRELATES WITH MEDICAL AND PSYCHIATRIC SYMPTOMS.**

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**Aims:** Rates of physical and sexual abuse in SUD patients vary greatly across studies. We examined prevalence rates in a diverse SUD sample and their medical/psychiatric correlates with goal of informing future practice.

**Methods:** Recruitment sites were 6 psychosocial & 5 methadone maintenance programs in NIDA CTN. Participants (N=628) met DSM-IV criteria for Drug Abuse/Dependence, reported recent unemployment/ underemployment and completed at least 30 days in treatment at baseline assessment. All subjects completed ASI Lite at baseline. Males and females with & without physical & sexual abuse (lifetime) were compared on a variety of medical & psychiatric measures with chi-square analyses.

**Results:** Women reported higher rates of physical (60.9%) & sexual (47.9%) abuse (lifetime) than men (24.7% and 12.5%, respectively, both  $p < .001$ ). Men & women with physical abuse were more likely to report recent depression ( $p < .008$ ); lifetime depression ( $p < .002$ ) & trouble controlling violent behavior (lifetime) ( $p < .001$ ). Men with physical abuse were more likely to report chronic medical problems (73%) than men without abuse (51%) ( $p < .001$ ). Rates were comparable for women with and without abuse. Similar patterns were seen for men and women with and without a sexual abuse history. Those with sexual abuse reported higher rates of recent and lifetime depression and trouble controlling violence (lifetime).

**Conclusions:** Women with SUDs report physical and sexual abuse at rates twice those of men. History of physical or sexual abuse was associated with increased rates of depression and trouble controlling violence in both genders. Men with physical abuse were more likely to present for treatment with a chronic medical problem. The constellation of problems suggests both men and women with histories of abuse would benefit from psychiatric evaluation and ancillary intervention services.

**Support:** NIDA CTN (Mid-Atlantic Node)

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**ILLICIT DRUG USE AND DEPENDENCE AMONG PATIENTS REFERRED TO A HEPATOLOGY CLINIC IN AN URBAN ACADEMIC MEDICAL CENTER.**

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**Aims:** Five million people in the United States are estimated to be seropositive for Hepatitis C Virus (HCV), the most common chronic bloodborne infection. Injection drug use is the most common mode of transmission for HCV, accounting for 68% of current infections in the USA. The Kreek-McHugh-Schulger-Kellog Scale (KMSK) quantifies self-reported lifetime use of heroin and illicit opiates and cocaine, as well as alcohol and tobacco. Patients referred to an urban tertiary care academic medical center hepatology clinic primarily treating patients with HCV and HBV were asked to complete the KMSK.

**Methods:** The KMSK was self-administered by 193 consecutive patients who presented for evaluation of liver disease during a 19 month period. (Kreek et al, Drug Alcohol Depend, 2003)

**Results:** Of the 193 patients, 179 patients had questionnaires available; of the 179, 86 reported some use of cocaine, 69 reported no use, and 24 failed to fill out information. Of the 86, 60 gave complete data, which allows quantification. Of these 60 patients, 39 met KMSK criteria for cocaine dependence (cutoff score  $\geq 11$ ). Of the 179 patients, 82 reported some use of heroin or other illicit opiates, 69 reported no use, and 28 failed to fill out information. Of the 82, 62 gave complete data. Of these 62 patients, 41 met KMSK criteria for opiate dependence (cutoff score  $\geq 9$ ). Of the 57 patients meeting criteria for dependence on either drug, 23 were codependent.

**Conclusions:** Drug use and dependence was very high among the patients referred to an urban tertiary care academic medical center hepatology clinic. Lifetime use in the general populace is 14.5% and 1.5% for cocaine and heroin respectively, but use in our sample was 56% and 57%. Therefore hepatology clinics are potentially valuable sites to offer colocated outreach and treatment to those with hepatitis and addiction.

**Support:** NIH-NIDA P60DA05130 and NYOASAS

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**INVOLVEMENT OF BASOLATERAL AMYGDALA DOPAMINE D1 AND D2 RECEPTORS ON THE EXPRESSION OF COCAINE-INDUCED CONDITIONED PLACE PREFERENCE IN RATS.**

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**Aims:** We investigated the role of dopamine D1 and D2 receptors in the basolateral amygdala (BLA) in the expression of conditioned place preference (CPP) of cocaine in rats.

**Methods:** Male Sprague-Dawley rats, weighing 300-350 g, were bilaterally implanted with stainless-steel guide cannulae 1 mm above the BLA (AP: -2.8 mm, ML:  $\pm 5.0$  mm, DV: 7.6 mm, from the bregma) after the establishment of place preference conditioned by cocaine. After the recovery, microinjection tests with antagonists were conducted for 3 consecutive days. On the 1st test day, all animals were injected with the vehicle (saline). On the next day, rats were injected with SCH23390 (2  $\mu$ g/1  $\mu$ l/side,  $n=10$ ), raclopride (5  $\mu$ g/1  $\mu$ l/side,  $n=8$ ) or vehicle ( $n=12$ ). On the 3rd day, vehicle was injected again to all of the animals. Then, daily 2 extinction sessions were conducted for 3 consecutive days. After a total of 6 extinction sessions, microinjection tests with agonists were conducted for 2 consecutive days. On the 1st day, all of the animals were injected with vehicle into the BLA. On the next day, the animals received microinjection of SKF38393 (5  $\mu$ g/1  $\mu$ l/side,  $n=10$ ), quinpirole (3  $\mu$ g/1  $\mu$ l/side,  $n=9$ ) or vehicle ( $n=10$ ) into the BLA prior to the CPP test.

**Results:** All animals were still significant expression of CPP, compared with pre test session. However, Microinjection of both D1 and D2 antagonist significantly inhibited the expression of CPP compared to vehicle. In addition, CPP was observed again on the 3rd test day. While, microinjection of D1 (but not D2) receptor agonist reinstated place preference after the extinction of CPP.

**Conclusions:** The present study demonstrated that the dopamine receptors in the BLA regulate approaching behavior to the environment that previously associated with the rewarding effect of cocaine.

**Support:** Shimojo Implicit Brain Function Project, Japan Science and Technology Agency.

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**THERMOREGULATORY AND BEHAVIORAL EFFECTS OF MDMA IN FLINDERS SENSITIVE LINE RATS.**

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**Aims:** 3,4-Methylenedioxymethamphetamine (MDMA, ecstasy) is a commonly used drug in the community associated with unpredictable and sometimes fatal increases in body temperature. It has also been associated with depressive mood states in users. Flinders Sensitive Line (FSL) rats represent a rat model of depression. They were originally bred from Sprague-Dawley (SD) rats, and are more sensitive to both muscarinic and serotonergic agonists. FSL rats have also been shown to have altered thermoregulatory responses to various drugs but the effect of MDMA in these animals has not been investigated.

**Methods:** 8 FSL and 8 SD rats were administered saline, and 5 and 7.5 mg/kg MDMA once each, with each dose given 1 week apart. Rats were 7 weeks old at the time of surgery to implant telemetry devices which measured core temperature (TC), heart rate and locomotor activity throughout the experiments. Immediately following saline or drug administration, rats were confined to an area with ambient temperature (TA)  $30 \pm 1^\circ\text{C}$  for 30 minutes, before being allowed access to a thermal gradient for four hours to behaviorally control TC. Brains were removed one week after final dose of MDMA and concentrations of serotonin, dopamine and their main metabolites were measured.

**Results:** Treatment with MDMA at both doses led to a higher TC in FSL rats than SD rats after the 30 minutes at high TA. Two of the 8 FSL rats did not survive the hyperthermia after the 5 mg/kg dose, and a further three out of the remaining six rats did not survive the 7.5 mg/kg dose. All but one of the SD rats recovered well. There were no significant changes in neurotransmitter concentrations in SD rats, but FSL rats showed significant decreases in all transmitters measured.

**Conclusions:** The results so far indicate that FSL rats may be more susceptible to developing MDMA-induced hyperthermia and possible damage to the brain. The importance of these results to human users of MDMA who also have depression is under investigation.

**Support:** This work was supported by NHMRC of Australia.



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### THE NEGATIVE PROGNOSTIC IMPACT OF CANNABIS DEPENDENCE IN A STUDY OF PATIENTS WITH BIPOLAR DISORDER AND SUBSTANCE USE DISORDERS.

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**Aims:** To determine whether cannabis dependence has a negative prognostic impact in a treatment study of patients with bipolar disorder (BD) and substance dependence.

**Methods:** Patients entering a treatment study of Integrated Group Therapy (IGT) for bipolar and substance use disorders were assessed at baseline, and then monthly throughout the 15-month follow-up period. Patients were randomly assigned to either IGT or group drug counseling and treated during the first three months of this period. Cannabis dependence was assessed using the Structured Clinical Interview for DSM-IV (SCID) and substance use was assessed using the Addiction Severity Index (ASI).

**Results:** In these analyses, 20 patients of 61 patients total met criteria for current cannabis dependence at baseline. Marijuana dependent patients were less likely to abstain from substance use during the 3 months of treatment, compared to patients not dependent on marijuana: they were half as likely to abstain for at least one treatment month (35.0% vs. 65.9%) and none of them abstained throughout treatment (0% vs. 36.6%).

**Conclusions:** The presence of cannabis dependence is a negative prognostic factor among patients with BD and substance dependence; those with cannabis dependence in our study were less responsive to behavioral treatment than the general study population.

**Support:** Supported by NIDA Grants R01 DA15968, K24 DA022288

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### PSYCHOSOCIAL FUNCTIONING IN METHADONE AND NONMETHADONE MAINTAINED PREGNANT WOMEN: RELATIONS TO TREATMENT ENGAGEMENT AND RETENTION.

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**Aims:** Poor treatment retention is a major problem among drug-dependent pregnant women. The present study examined the association between the current use of methadone and against medical advice (AMA) treatment dropout and assessed predictors for AMA dropout among pregnant drug-dependent patients in residential treatment.

**Methods:** This cross-sectional study utilized data on pregnant clients entering treatment at the Center for Addiction and Pregnancy (CAP), in Baltimore MD from February 1996 to August 1998. Univariate and multivariate logistic regression analyses were used to examine the association between methadone status and AMA treatment dropout from 7 days of residential care among the combined treatment population (N = 327). The data was also stratified into methadone (n = 126) and non-methadone (n = 201) patient groups to determine predictors for AMA treatment dropout.

**Results:** Despite the availability of comprehensive services 26% of the CAP treatment population left AMA. Opioid-dependent clients receiving methadone were 63% less likely to leave residential treatment than clients receiving abstinence-based treatment (OR = 0.37, 95% CI: 0.20, 0.66). Among clients receiving abstinence-based treatment, age (OR = 0.93, 95%CI: 0.88, 0.99), patient rating for the importance of drug treatment (OR = 0.45, 95% CI: 0.22, 0.90), and interviewer severity rating for family/social problems (OR = 0.85, 95% CI: 0.74, 0.98) were found to significantly decrease the odds of leaving AMA.

**Conclusions:** This study confirmed methadone's contribution to treatment retention among pregnant patients in a comprehensive treatment program. This study also identified patient factors which are associated with AMA treatment dropout from abstinence-based residential care including age, motivation, and family/social problems. Health care professionals should be aware of the benefits of methadone maintenance therapy to ensure that women who qualify can benefit from this therapeutic adjunct.

**Support:** Supported by NIDA R01DA022081.

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### ALPHA-2A ADRENOCEPTORS PLAY A ROLE IN BEHAVIORAL FLEXIBILITY IN MICE, BUT ARE NOT REQUIRED FOR IMPROVEMENTS CAUSED BY ATOMOXETINE.

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**Aims:** Behavioral inflexibility is thought to be a key component of the acquisition and maintenance of substance dependence disorder. Recent studies from our lab indicate that atomoxetine, and other inhibitors of noradrenaline reuptake, enhance behavioral flexibility in mice, rats and monkeys. Nevertheless, the mechanisms by which increased catecholamine signaling produce this effect are unknown.

**Methods:** Alpha-2A receptors have been implicated in working memory performance; to further characterize the role of this receptor in other forms of cognitive control, we studied operant serial reversal learning in homozygous alpha-2A null mutants, heterozygotes and wild-type littermate mice. Animals were initially trained on a simple rule (e.g., respond to the left aperture to get reward). On the following day, the spatial discrimination was reversed; mice performed under this condition over consecutive days until the same criterion was met. In a second study, saline or atomoxetine (1.0 mg/kg, s.c.) was administered 30 minutes before all first reversal sessions.

**Results:** While there was no significant effect of genotype on trials required to reach criterion during acquisition of the initial aperture-reward association, homozygotes required significantly more trials than wild-types on during the first, and heterozygotes exhibited an intermediate impairment. The second study replicated these results for homozygotes and wild-type mice, and showed that atomoxetine reduces trials to reach criterion in both genotypes.

**Conclusions:** These results reveal an alpha-2A gene-effect that is specific to the the first reward contingency reversal. Additionally, they indicate that atomoxetine improves behavioral flexibility in this task, but that its effects are not fully dependent on the alpha-2A receptor; its effects may be larger in homozygote mutants than in wild-type animals, which could be due either to the lower baseline performance of homozygotes, or could be a direct result of the null mutation itself.

**Support:** P50-MH77248

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### PRE-QUIT BRAIN FMRI RESPONSES TO TOBACCO SMOKING-RELATED CUES PREDICT SLIPS DURING SMOKING CESSATION TREATMENT.

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**Aims:** In tobacco smokers attempting to quit, slips are predictive of future relapse (Borland, 1990; Ockene et al., 2000; Wileyto et al., 2004). Slips can be precipitated by a number of factors, including smoking-related cue exposure (Borland, 1990). Developing means to predict slips prior to cessation may help direct treatment of vulnerable smokers. We used functional MRI (fMRI) to determine whether pre-quit cue reactivity is predictive of future slips.

**Methods:** Thirteen nicotine-dependent women aged 43.2 ± 11.5 years old were scanned prior to quitting and then were treated with nicotine replacement therapy (NRT) and cognitive behavioral therapy. Six subjects slipped during NRT treatment while 7 maintained continuous abstinence. Pre-quit Fagerstrom test scores for nicotine dependence and expired carbon monoxide levels were equivalent in both groups. Functional MRI scans acquired with a Siemens 3T scanner involved presentation of neutral and smoking-related cues adapted from Due et al. (2002). Data were analyzed with BrainVoyagerQX 1.10 and whole brain fixed effects analysis was run comparing brain responses to smoking-related versus neutral cues between subjects who did and did not slip. Multiple comparisons were corrected using a group voxel statistical threshold of  $t = 3.1$   $p < 0.01$ .

**Results:** Subjects who ultimately slipped exhibited greater cue-induced activation in the insula, frontal cortex, amygdala, caudate nucleus, and substantia nigra. Those regions are involved in stimulant craving, impulsivity, and emotional and habitual responding.

**Conclusions:** Our findings suggest that enhanced pre-quit fMRI cue reactivity in those areas may identify smokers at increased risk for experiencing slips while on NRT and may predict which smokers might benefit from alternative smoking cessation treatments.

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### EFFECTS OF CATECHOLAMINE REUPTAKE INHIBITORS AND MODAFINIL ON METHAMPHETAMINE SELF-ADMINISTRATION IN RATS.

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**Aims:** Catecholamine reuptake inhibitors have emerged as candidate medications for the treatment of methamphetamine (MA) dependence. Bupropion reduces MA's stimulus effects in humans (Newton et al. 2006) and MA self-administration in rats (Reichel et al. 2008), but its clinical efficacy in MA dependence is in question (Shoptaw et al. 2008). We examined the effects of a low dose of bupropion on self-administration of MA. We further sought to determine whether any observed effects depended more upon inhibition of noradrenergic or dopamine reuptake.

**Methods:** Adult male rats were trained to self-administer MA (0.025 mg/kg/infusion) on an FR2 schedule of reinforcement. Next, each rat was randomly allocated to various doses of MA (0, 0.001, 0.01 or 0.1 mg/kg/infusion). In each week, they were stabilized on a dose of MA for 2-3 days before being tested for self-administration of that same dose after treatment with placebo or an active drug (given in a counter-balanced order over two consecutive days). The active drugs used included bupropion (20 mg/kg, s.c.), atomoxetine (1 mg/kg, i.p.), GBR-12909 (10 mg/kg, i.p.) and modafinil (10 mg/kg, i.p.).

**Results:** Bupropion increased responding when low doses of MA were available, or during extinction, and decreased responding supported by optimal or higher doses (>0.01 mg/kg/infusion). Atomoxetine lessened responding during extinction or in a progressive ratio test, but did not consistently affect active self-administration; modafinil and GBR-12909 were without any observed effects.

**Conclusions:** A low dose of bupropion produced a right-ward shift in the dose-response curve for MA self-administration. While atomoxetine did not reduce active self-administration, it did lessen responding in extinction and during a progressive ratio test, perhaps indicating that it enables active suppression of responding. Future experiments should be done to test whether atomoxetine is a preferred pharmacological strategy for enabling voluntary cessation of MA-taking behavior.

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### ANXIOUS AROUSAL AND ANHEDONIC DEPRESSION SYMPTOMS AND THE FREQUENCY OF CURRENT MARIJUANA USE: TESTING THE MEDIATING ROLE OF MARIJUANA USE COPING MOTIVES AMONG ACTIVE USERS.

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**Aims:** The present investigation sought to examine anxious arousal and anhedonic depression symptoms in relation to the frequency of past 30-day marijuana use, as well as the role of marijuana use coping motives in terms of mediating this relation.

**Methods:** Participants consisted of 154 community recruited young adult (48.1% female; Mage = 20.75, SD = 5.97) current marijuana users. Participants were eligible for enrollment in the present study if they endorsed marijuana use within the past 30 days and were between the ages of 18 and 65 years. If deemed eligible for participation, participants completed a battery of self-report measures. At the completion of the study, participants were debriefed and compensated \$20 for their time.

**Results:** After controlling for daily cigarette smoking rate, alcohol consumption, and gender, anxious arousal symptoms [ $t = 2.24$ ,  $\beta = .19$ ,  $p < .05$ ], but not anhedonic depression symptoms [ $t = .19$ ,  $\beta = .02$ ,  $p = ns$ ], were significantly and uniquely associated with the frequency of marijuana use. In addition, coping motives for marijuana use mediated the relation between anxious arousal symptoms and frequency of current marijuana use.

**Conclusions:** The present study provides novel empirical information concerning anxious arousal, anhedonic depression, and marijuana coping motives in terms of their relation to the frequency of marijuana use. These present data point to the possible relevance of coping motives for marijuana use as a theoretically viable mechanism within an anxiety-marijuana use relation.

**Support:** This work was supported by National Institute on Drug Abuse research grants (1 R01 MH076629-01, 1 R01 DA018734-01A1, and R03 DA16307-01) awarded to Dr. Zvolensky. Dr. Bonn-Miller also acknowledges that this work was supported in part by VA Office of Academic Affairs and Health Services Research and Development Service Research funds.

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### REDUCTIONS IN HEROIN USE FREQUENCY FOLLOWING HURRICANE KATRINA.

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**Aims:** This paper analyzes how New Orleans heroin users coped with the difficulties during Katrina, at their evacuation sites, and whether they continued heroin use when settled in New Orleans or Houston. Many drug users in New Orleans experienced a multitude of disruptions and difficulties during the week (Aug. 30-Sept 5, 2005) following Hurricane Katrina, as well as difficulties in adjusting to their evacuation sites. Several returned to New Orleans in 2006 and 2007, and encountered a resurgent drug market.

**Methods:** This NIDA-funded study documents the impacts of disruption of illegal drug markets among New Orleans Evacuees. This paper provides findings from 107 New Orleans evacuees who completed in-depth qualitative interviews where questions elicited rich stories about their drug use in New Orleans and Houston. This paper focuses on reports of 25 subjects who self-reported using heroin during one or more of four window periods: month before Katrina, whether and how they used during the Katrina Week, in the month following evacuation, and at interview a year or more later.

**Results:** Prior to Katrina over two-thirds reported being daily heroin users and few were non-heroin users. The hurricane and flooding of New Orleans severely disrupted daily heroin use patterns; nearly two-thirds reported nonuse of heroin during the flooding with varied reasons mentioned. Likewise, heroin nonuse was almost equally common during the month or so following evacuation to new locations; daily heroin use was quite uncommon. Daily use had not returned for most heroin users a year or two after Katrina, but few reported a clear intent to never heroin use again.

**Conclusions:** New Orleans evacuee heroin users reported numerous difficulties and deprivations following Katrina. These difficulties dominated their lives and were more important to them than a need to pursue and use heroin—which was often unavailable, hard to find, and quite expensive.

**Support:** NIDA grants: (R01 DA021783-04) and Behavioral Science Training in Drug Abuse Research (T32 DA007233-25).

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### EFFECTS OF ACUTE ORAL CAFFEINE PRETREATMENT ON RESPONSE TO INTRAVENOUS NICOTINE AND COCAINE IN STIMULANT USERS.

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**Aims:** A previous study in stimulant users showed oral caffeine maintenance increased some measures of stimulant and reinforcing effects in response to intravenous nicotine. Caffeine also increased dollar value of nicotine (2 mg/70 kg) in a drug vs. money procedure. The present study examined whether acute oral caffeine pretreatment alters subject-rated effects, monetary value, and physiological effects resulting from intravenous nicotine in participants who were regular users of caffeine, tobacco, and cocaine. To determine whether any relationships would be pharmacologically specific to nicotine, the effects of acute oral caffeine in response to intravenous cocaine were also studied.

**Methods:** Fourteen (1 female) volunteers participated in this approximately 3-4 week, double-blind, inpatient study. Volunteers participated in 10 experimental conditions in pseudorandomized order, in which oral caffeine (250 mg/70kg) or placebo was administered 1 h before an intravenous injection, which consisted of nicotine (1 or 2 mg/70 kg), cocaine (15 or 30 mg/70 kg), or saline. Outcome measures included subject-rated and physiological variables.

**Results:** Acute caffeine administration attenuated the increase in the following subject-rated items resulting from 2 mg/70 kg nicotine administration: "rush," "drug effect," "good effects," "liking," "high," and "calm/relaxed". Caffeine had no effect on ratings of "bad effects" resulting from nicotine. Caffeine potentiated nicotine-induced blood pressure increase, but reduced nicotine-induced heart rate increase. Caffeine did not significantly alter the value of nicotine in a drug vs. money choice procedure. In contrast to the effects of caffeine on response to nicotine, acute caffeine either augmented or had no significant effect on subject-rated and physiological response to cocaine.

**Conclusions:** In contrast to the previous maintenance study, these data suggest acutely administered caffeine may decrease nicotine abuse liability.

**Support:** Funding by NIDA grants DA03890, DA023186, and DA07209.

# EVALUATION OF PLASMA NALTREXONE CONCENTRATIONS RESULTING FROM USE OF ALO-01 (MORPHINE SULFATE EXTENDED-RELEASE WITH SEQUESTERED NALTREXONE HYDROCHLORIDE) CAPSULES FOR CHRONIC PAIN.

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**Aims:** ALO-01 (morphine sulfate extended-release with sequestered naltrexone hydrochloride) Capsules are under development for relief of chronic moderate to severe pain.<sup>1</sup> If tampered with (crushed/chewed), sequestered naltrexone is released to mitigate morphine-induced euphoria.<sup>2,3</sup> Hypothesis: naltrexone exposure would be minimal in patients with chronic moderate to severe pain taking ALO-01 Capsules in a 12mo open-label safety trial.

**Methods:** Samples were drawn to measure plasma concentrations (concs) of morphine (M), naltrexone (N), and its metabolite 6- $\beta$ -naltrexol (6- $\beta$ -N) just before dosing during monthly visits in a subset of study participants. Limits of quantification were 0.200ng/mL, 4.00pg/mL, and 0.250pg/mL, respectively. Withdrawal symptoms were assessed using Clinical Opiate Withdrawal Scale (COWS).<sup>4</sup>

**Results:** In 93 patients, M concs ranged from 18.6-26.9ng/mL. Twenty-one patients (22.6%) had at least 1 quantifiable N conc; overall, 49/444 (11%) samples were quantifiable (range, 4.03-145pg/mL). Median N conc in patients with quantifiable levels was 10.1pg/mL (over all samples, median was 0). For 6- $\beta$ -N, 74 patients (79.6%) had  $\geq 1$  quantifiable level; 338/457 samples (74.0%) were quantifiable (range, 0.471-3720 pg/mL); median of quantifiable levels was 18.5pg/mL. Four patients had  $\geq 1$  outlying N conc ( $>1SD$  of mean); however, patients with a quantifiable N level did not have an increase in COWS score or decrease in pain relief. Analyses did not reveal evidence of accumulation of N and 6- $\beta$ -N nor association with dose, age or gender.

**Conclusions:** Results suggest when ALO-01 Capsules are taken as directed for chronic moderate to severe pain, steady state plasma morphine levels remain stable. Naltrexone and 6- $\beta$ -N do not accumulate; small amounts, when detected, were not dose related and not associated with clinically observable effects of opioid withdrawal or reduction of pain relief.

1JPain.2008;9(S1):41, 2Ibid:35, 3Ibid:34, 4JPsychoactiveDrugs.2003;35:253-9

**Support:** Alpharma Pharmaceuticals LLC

# ADDICTION TO FOOD: THE RELATIONSHIP BETWEEN DELAY DISCOUNTING, OBESITY, AND THE BINGE EATING SCALE.

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**Aims:** Obesity, as a result of eating dysfunction, shares many common features with addiction including loss of control and negative consequences. Measures of impulsivity have frequently been used to study addiction (Bickel & Marsch, 2001), but only recently been applied to the study of obesity (Weller et al., in press). Measures of delay discounting have not explored eating dysfunction (binge eating) specifically. This study explores the relationship between self-reports of impulsivity and delay discounting on measures of obesity and binge eating.

**Methods:** Sixty-three women completed a three-session study where they completed multiple measures of hypothetical delay discounting of several commodities (hypothetical money, exercise, and preferred food), one real money discounting measure, and self-report measures of impulsivity (Barratt Impulsivity Scale (1985) and Stanford Time Perception Inventory). Body mass index (BMI) and a binge eating scale (BES) were collected as measures of eating dysfunction.

**Results:** Hypothetical commodities of discounting were well described by the Mazur (1987) hyperbolic discounting function. Rates of discounting of real money were significantly correlated with BMI ( $r(61) = .269$ ,  $p = .036$ ) and almost significantly correlated with BES ( $r(56) = .248$ ,  $p = .056$ ). Rates of discounting also correlate with some subscales of self-report impulsivity but not with others.

**Conclusions:** This study confirms the notion that eating dysfunction is a form of addiction. We propose that binge eating and obesity are related to impulsive decision-making and that rates of discounting might be an indicator of which individuals might benefit from direct intervention of unhealthy eating habits.

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# MULTIDIMENSIONS OF HIV RISK FOR DRUG-DEPENDENT PREGNANT PATIENTS.

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**Aims:** 1) Determine the extent to which the seven ASI composite scores (CS) predict HIV drug and sex risk behaviors; 2) Determine if such a prediction is common to the same or a unique set of ASI CSs; 3) Examine the extent to which individual items within the predictive ASI CSs account for prediction of drug and sex risk; 4) Evaluate the multidimensional aspects of risk and protective factors by categorizing participants into four groups of HIV risk behaviors: low risk for both drug and sex, risk for drug but not sex, risk for sex but not drug, and risk for both drug and sex—and examine the extent to which ASI CSs and individual items within those scores predict these categories.

**Methods:** Pregnant women entering a behavioral study to reduce drug use ( $N=76$ ) completed pretreatment ASI and HIV risk questionnaires.

**Results:** The total sample was 57% non-White; 70% used opioids and 70% used cocaine in the month prior to treatment. Only the Legal CS significantly predicted HIV sex risk behaviors ( $p < .01$ ). Both the Legal and Drug CSs were significant predictors of drug risk behaviors (both  $ps < .01$ ). For sex risk, the individual Legal item, charged with prostitution, significantly predicted sex risk scores ( $p = .04$ ). For drug risk, no Legal items examined significantly predicted drug risk scores. Within the Drug CS, past 30-day frequency and route of heroin use were significant predictors of drug risk ( $p = .01$  and  $.04$ , respectively). Examining the means of the four risk groups indicated that regardless of HIV drug-risk behavior, women with high risk for HIV sex behaviors had more severe CSs on most ASI domains. Further, the combination of high risk for both HIV drug-risk and sex-risk behaviors did not appear to be synergistic in terms of ASI composite severity compared with the other groups.

**Conclusions:** The ASI is a helpful tool for screening pregnant substance abuse treatment patients for HIV risk behavior. Treatment should be tailored to address the multiple dimensions of HIV risk in drug-dependent pregnant patients, with particular attention to HIV sex-risk behaviors.

**Support:** NIDA RO1 DA14979

# IMPACT OF CYP2D6 GENOTYPE ON THE PHARMACODYNAMIC EFFECTS OF OXYCODONE IN HUMANS: A RETROSPECTIVE ANALYSIS.

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**Aims:** Oxycodone, a widely prescribed opioid for the treatment of moderate to severe pain, is commonly abused. The primary means of oxycodone metabolism is the hepatic enzyme P450 (CYP) 2D6. The gene responsible for the production of this enzyme (CYP2D6) has been shown to be highly polymorphic, resulting in distinct functional phenotypes. Poor metabolizers (PM) of CYP2D6 substrates, including oxycodone, have been shown to comprise as much as 7% of certain ethnic populations. Despite the frequency of this phenotype, the impact of reducing metabolizing enzyme activity on the subjective and therapeutic effects of oxycodone has yet to be determined. Because variation in drug pharmacokinetics can lead to divergent drug responses, the present study sought to evaluate the effects of oxycodone in poor and normal metabolizers.

**Methods:** In another investigation by this laboratory, the effects of oxycodone were examined in prescription opioid abusers and others with a history of medicinal opioid use. Throughout a total of twelve sessions, the effects of orally administered oxycodone (0, 15, 30 mg/70 kg) were examined. For the purposes of the current study, the data obtained from these measures were re-examined in order to uncover differences between participants who were poor ( $n=7$ ) versus normal ( $n=11$ ) metabolizers.

**Results:** Although oxycodone produced significant dose-dependent effects in both groups, poor and normal metabolizers did differ in the intensity of their subjective ratings of Nausea ( $p<.001$ ), Drug Quality ( $p<.05$ ), Good Drug Effect ( $p<.05$ ), and amount of money they would pay for the drug ( $p<.05$ ).

**Conclusions:** These results suggest that differential metabolism of oxycodone by CYP2D6 can lead to divergent drug responses. Specifically, poor metabolizers may be hypersensitive to many of oxycodone's effects. It is important to investigate the influence of such pharmacogenetic interactions since a drug's subjective profile can significantly contribute to its abuse potential.

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### BEHAVIORAL CHARACTERIZATION OF NOVEL NICOTINIC RECEPTOR COMPOUNDS BASED ON THE STRUCTURE OF CYTISINE.

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**Aims:** Partial nicotinic receptor agonists, such as cytisine and varenicline, are used as smoking cessation treatments. The present study further characterized the pharmacological properties of cytisine, varenicline, and a number of cytisine-related compounds (CC5, CC7, and Cmpd20) (Canu Boido and Sparatore, 1999; Carbonnelle et al., 2003). It was hypothesized that these compounds would have partial agonist activity at nicotinic receptors and attenuate the discriminative, but not the convulsive effects, of nicotine.

**Methods:** For these studies, male Sprague-Dawley (N=12) rats were trained to discriminate nicotine or cytisine from saline, and convulsions were evaluated in naïve ICR mice following injections of nicotine or cytisine.

**Results:** In rats trained to discriminate a low dose of nicotine (0.32 mg/kg salt), cytisine partially generalized to nicotine. Varenicline and CC5 produced greater generalization to the discriminative properties of cytisine than to nicotine. CC7 and Cmpd20 did not engender any nicotine- or cytisine-like responding. Cytisine, CC5, CC7, and Cmpd20 partially blocked the discriminative effects of nicotine, but only Cmpd20 partially antagonized the discriminative effects of cytisine. In addition, these compounds failed to block significantly the convulsive effects of nicotine. CC5 demonstrated some preconvulsant activity on its own, but did not potentiate the convulsant effects of nicotine.

**Conclusions:** Cytisine, varenicline, and CC5 all demonstrated some partial agonist activity at the nicotinic receptor, while CC7 and Cmpd20 demonstrated only antagonist properties. These studies demonstrated that the cytisine structure can be modified to produce compounds that behaviorally resemble partial agonists and antagonists.

**Support:** These studies were supported by USPHS grant T32 DA007268 and the University of Michigan Tobacco Research Network.

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### MDMA USE IS ASSOCIATED WITH INCREASED BASAL GANGLIA-THALAMOCORTICAL CIRCUIT ACTIVATION DURING MOTOR TASK PERFORMANCE IN HUMANS: AN FMRI STUDY.

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**Aims:** MDMA (3,4-methylenedioxymethamphetamine; Ecstasy) is a popular recreational drug that produces long-lasting serotonin (5-HT) neurotoxicity. 5-HT innervates cortical and sub-cortical brain regions mediating motor function, suggesting that MDMA users may have altered motor system neurophysiology. We used functional magnetic resonance imaging (fMRI) to assay motor task performance-associated brain activation changes in MDMA and non-MDMA users. **Methods:** 24 subjects (14 abstinent MDMA users and 10 controls) performed an event-related motor task (1, 2 or 4 taps) during fMRI on a 3 Tesla scanner. Subjects were instructed to tap their right index finger according to a visual display. Motor regions of interest were used to measure PSC and PAV in the bilateral motor cortex, sensory cortex, supplementary motor area (SMA), caudate, putamen, pallidum and thalamus. Data was analyzed with SPM5 employing standard techniques. Brain activation was measured via three methods: T-maps, percent signal change (PSC) and percent activated voxels (PAV).

**Results:** There was no statistically significant difference in reaction time between the two groups. For the 4-Tap condition, MDMA had more activation than controls in the right SMA for T-score ( $p=0.04$ ), PSC ( $p=0.04$ ) and PAV ( $p=0.03$ ). Lifetime episodes of MDMA use were positively correlated with PSC for the 4-Tap condition on the right for putamen and pallidum; with PAV in the right and motor and sensory cortex and bilateral thalamus.

**Conclusions:** We found a group difference in the right SMA and positive dose-response association between lifetime exposure to MDMA and signal magnitude and extent in several brain regions. This evidence is consistent with altered 5-HT signaling in basal ganglia-thalamocortical circuits. Further studies examining behavioral correlates and the specific neurophysiological basis of the observed findings are warranted.

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### NEONATAL ABSTINENCE SYNDROME AND GENDER: DOES SEX MATTER?

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**Aims:** Neonatal abstinence syndrome (NAS) has been reported to occur among 60-90% of infants exposed to opioids in utero. However, there is significant variability in onset, severity of withdrawal and length of treatment. For those infants whose mothers receive methadone, the picture is more confusing as studies suggest no relationship between maternal methadone dose and duration of methadone exposure. Recent efforts have been directed at delineating factors that may account for such variability and there has been anecdotal evidence gender may play a role. The purpose of this study is to examine the effect of gender on NAS in a large sample of infants born exposed to methadone.

**Methods:** A secondary analysis was conducted on a perinatal data set that includes data infants born to women enrolled in a comprehensive methadone treatment program. The use of the data base was approved by the Thomas Jefferson University IRB. Data was available for 412 infants, 209 females and 203 males born between 2004 and 2008. Statistical analyses included chi square and OLS multiple regressions.

**Results:** Of the 412 infants, 243 (59%) required treatment for NAS. Chi square revealed no difference between males and females requiring treatment ( $\chi^2=0.2993, p=0.584$ ). OLS multiple regression revealed no relationship between gender and length of NAS treatment but did find a relationship between length of treatment and birthweight ( $p<.000$ ); however when EGA was entered into the model of length of treatment, gender, birthweight and EGA, only EGA was significant ( $p=.01$ ). Multiple regressions with the highest dose of treatment and gender also found no significant differences.

**Conclusions:** These findings provide strong evidence that the severity of NAS does not differ as a function of gender. The relationship of EGA to NAS is expected, as the incidence of NAS in premature infants is much less than in term infants. The size of the sample in this study is unique in that it is the largest reported sample of methadone exposed infants.

**Support:** This research is supported by the research division of Maternal Addiction Treatment Education and Research, Department of Pediatrics, Thomas Jefferson University.

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### RISK BEHAVIORS OF A SAMPLE OF FEMALE INJECTION DRUG USERS IN MALAYSIA.

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**Aims:** A subsample of female IDUs was analyzed to identify their characteristics, drug use histories, and risk behaviors.

**Methods:** The survey utilized a purposive sampling technique and enrolled not in treatment IDUs in high drug use neighborhoods. Anonymous survey data was collected by trained interviewers using a face to face structured interview. Urine toxicology for methamphetamine, morphine, benzodiazepine and buprenorphine was carried out

**Results:** Female IDUs ( $n=26$ ) constituted 10% of the total number of IDUs sampled ( $N=250$ ); 54% of the females (14/26) were of Malay ethnicity. Female IDUs had a mean (SD) age of 41.5 (7.7) years; 14/26 (54%) had less than 6 years of schooling. Female IDUs reported mean (SD) of 17 (7) years of heroin use and 5 (4) years of ATS use. All female IDUs had an opiate-positive urine toxicology; 11.5% (3/26) tested positive for benzodiazepine, and 65.4% (17/26) for methamphetamine. 9/26 (35%) reported sharing needles/works in the past 30 days. 14/26 (54%) reported sex work; 14/26 (54%) reported inconsistent or no condom use in the past 30 days. 8/26 (31%) reported being HIV+, 42% (11/26) reported testing HIV. 23/26 (89%) reported a history of at least one imprisonment for drug use and 21/26 (81%) reported a history of enforced detention in a residential facility for drug users; only 8/26 (31%) had been in any medication treatment program for their drug problem.

**Conclusions:** The high prevalence of current sharing of needles/works, sex work, and unprotected sex with multiple sex partners and high seroprevalence of HIV in this sample of female IDUs points to the urgent need to implement effective drug abuse treatment and other HIV risk reduction interventions targeting female IDUs. The emergence of ATS abuse in this population further complicates effective interventions. Only a minority (31%) of the female IDUs had ever received medication treatment (opioid antagonist or agonist maintenance)

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### RETENTION AND TRANSITION TO LONG-TERM TREATMENT IN OPIOID-DEPENDENT PATIENTS: IMPACT OF INTENSIVE ROLE INDUCTION.

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**Aims:** Most patients fail to transition from outpatient opioid detox to post-detox counseling. This study compared three counseling strategies for facilitating this transition.

**Methods:** Applicants to a 30-day buprenorphine detox at a community-based outpatient drug abuse program [ $N = 239$ ; 55% male; 92% African American; age  $M = 43.0$  ( $SD = 7.0$ )] were randomly assigned to: (1) Routine counseling (RC), (2) Intensive Role Induction (IRI) consisting of five individual weekly counseling sessions provided during detox (Katz et al., 2004;2008) and focusing on improving retention in detox and on transitioning to post-detox counseling; or (3) IRI + Case Management (CM) which added to IRI a focus on helping patients to obtain needed ancillary services.

**Results:** Logistic regression analysis indicated that IRI participants (68%) were significantly more likely than RC participants (49%) to complete detox ( $p = .02$ ). There was a greater tendency for IRI participants (54%) than RC participants (41%) to attend at least one post-detox session ( $p = .09$ ). Analyses of variance revealed that IRI ( $M = 3.4$ ,  $SE = 0.2$ ) and CM participants ( $M = 3.2$ ,  $SE = 0.2$ ), on average, attended significantly more counseling sessions during detoxification than RC participants ( $M = 2.0$ ,  $SE = 0.2$ ). IRI ( $M = 34.9$ ,  $SE = 4.7$ ;  $p = .01$ ), but not CM ( $M = 21.9$ ,  $SE = 4.9$ ; N.S.), participants were retained, on average, for significantly more days post-detox than were RC participants ( $M = 16.1$ ,  $SE = 4.6$ ).

**Conclusions:** IRI appears capable of increasing retention in detoxification, for enabling patients to complete detoxification, and for increasing the likelihood of transition into post-detox counseling. IRI also improved retention in treatment following detox. Further efforts are warranted to improve outcomes for opioid dependent individuals who chose detox.

**Support:** This research was funded by NIDA Grant RO1 DA 11402. We also thank Reckitt Benckiser for their generous support of this project.

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### EFFECTS OF THE COMBINATION OF METYRAPONE AND OXAZEPAM ON CUE-INDUCED REINSTATEMENT OF COCAINE SEEKING.

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**Aims:** Drug reinforcement is partly mediated through interactions with the hypothalamo-pituitary-adrenal (HPA) axis which is activated by both stress and exposure to stimulants. Compounds (i.e., metyrapone (Met) and oxazepam (Ox)) that block the HPA axis at different levels have individually been shown to attenuate ongoing drug self-administration (SA) as well as the reinstatement (Rein) of drug-seeking behavior. If the combination of low doses of Met and Ox reduces cue-induced cocaine seeking then their potential adverse side effects should be mitigated without diminishing the desired reduction in cocaine seeking. Therefore, this experiment investigated the effects of the combination of Met and Ox on the ability of cocaine-associated cues to reinstate cocaine-seeking behavior.

**Methods:** Male Wistar rats weighing ~335g were implanted with chronic jugular catheters and trained to SA cocaine (0.25 mg/kg/inf) paired with a tone and light stimulus during daily 2-h sessions. After 10 days at FR4 (with the last 3 varying less than 10%) the rats were placed into abstinence for 2 weeks. Cue-induced Rein was then tested on the 15th day. Rats were treated with four combinations (25 or 50 mg/kg Met and 5 or 10 mg/kg Ox) or vehicle 30 min before the start of a 2-h Rein test session. Two additional groups of rats were treated with the combo (50 mg/kg Met and 10 mg/kg Ox) or vehicle 30 min before the start of a 15-min Rein test session and sacrificed for analysis of brain tissue. Blood for corticosterone was drawn from all rats after the last day of SA, the last day of abstinence and after the Rein session.

**Results:** Pretreatment with combinations of Met and Ox attenuated cue-induced Rein. Corticosterone levels were not different among the seven groups.

**Conclusions:** These data suggest that the combination of Met and Ox may be useful in blocking the ability of environmental cues to stimulate cocaine seeking without affecting stress hormone levels, suggesting that they may be reducing cocaine seeking through an unknown mechanism.

**Support:** USPHS Grant DA06013 from the National Institute on Drug Abuse

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### DRUG COURT AND TREATMENT: AN ETHNOGRAPHIC EXPLORATION.

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**Aims:** This project describes the day-to-day practices of an urban drug court and one of its affiliated treatment programs. An analysis as to how "addiction" is defined by various involved parties is offered, as well as a discussion as to how defendants/clients relate to the treatment process.

**Methods:** Five months of ethnography were conducted in an urban, East Coast drug court, including six weeks examining the practices of the court's case managers. Eight additional months of ethnography were conducted at a modified therapeutic community that accepts clients from the court. Interviews were conducted with court officials and staff, as well as with treatment staff. An additional 60 interviews were conducted with clients.

**Results:** Presumably due to inequitable policing, 98% of the court's defendants are African-American or Latino, and almost all are members of the working-class, marginally employed, or unemployed. Court screening tends to send clients with secure housing and employment to out-patient facilities, while those in less stable situations are sent to residential facilities. Approximately half of the clients "bought into" the treatment plan, while the other half evidenced skeptical or even hostile attitudes. All clients appreciated the opportunity to remain out of jail, though a small minority came to regret their decision to participate. Within the treatment facility, job training was cited as the most appreciated benefit, with clients expressing a wide variety of opinion regarding the therapeutic practice. Aspirations to resolve issues concerning drugs were almost uniformly bound up with a client's desire for upward mobility.

**Conclusions:** Services related to class advancement (e.g. GED classes and job training) should be made more available without the need for arrest. Treatment protocols should be modified to take greater account of client hostility and to take better advantage of desires for upward mobility.

**Support:** New York University, Department of Social and Cultural Analysis; Behavioral Sciences Training in Drug Abuse Research, T32DA007233, Public Health Solutions

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### RELATIONSHIP BETWEEN PATIENT ATTITUDES TOWARD METHADONE AND METHADONE TREATMENT PROGRAM RETENTION.

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**Aims:** To examine the relationship between attitudes toward methadone measured at baseline, and 3, 6, and 12 months post-baseline and treatment retention in patients newly admitted to a methadone treatment program (MTP).

**Methods:** 191 opioid-addicted individuals in six MTPs were administered a revised version of the Attitudes toward Methadone Scale (AMS; Brown et al., 1972; Schwartz et al., 2008) at admission to the MTP and 3, 6, and 12 months following admission, regardless of their treatment retention status. The revised AMS consists of 28 items rated on a 5-point Likert scale with 5 indicating the most positive rating of methadone; responses were summed to provide a total score ( $\alpha = .81$ ). Regression analysis was conducted to investigate whether AMS means were significantly different at baseline among four groups of patients retained in treatment: 1) less than three months ( $n = 35$ ); 2) between three and six months ( $n = 17$ ); 3) between six and twelve months ( $n = 21$ ); and, 4) twelve months ( $n = 118$ ). A subsequent linear mixed model analysis was also conducted to explore group differences in attitudes over time in AMS scores. A follow-up mixed model analysis of AMS scores of the subset of patients who remained in treatment the entire year was additionally conducted to investigate whether attitudes changed significantly over time.

**Results:** There were no significant differences in attitudes toward methadone at baseline among the groups based on their length of stay in treatment. There were also no differences in attitudes toward methadone over time within groups or for those who remained in treatment for at least a year.

**Conclusions:** Attitudes toward methadone does not appear to play an important role in treatment retention.

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**EFFECT OF SEX AND ESTROUS ON CHOICE BETWEEN FOOD AND COCAINE IN MALE AND FEMALE RATS.**

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**Aims:** Some sex differences in drug-taking behavior may be explained by changes in behavior across the female reproductive cycle. Estrus female rats exhibit higher operant responding for cocaine reinforcement than males or nonestrous females. In contrast, estrus females exhibit lower operant responding for food reinforcement than do males or nonestrous females. This suggests that the estrous cycle differentially influences food and cocaine motivation. The present study examines the effect of sex and estrous cycle on the motivation for food versus cocaine during an alternative reinforcement procedure.

**Methods:** Male and female Sprague Dawley rats were trained to respond on the "food" lever for food on a FR1 (20s TO) reinforcement schedule and were trained to respond on the "cocaine" lever for cocaine (0.4 mg/kg/0.1 ml infusion/4 sec) on a FR1 (20s TO)—during training sessions only 1 lever was extended with the available reinforcer alternating between successive sessions. After training, rats received discrimination tests (FR1 20s TO) during which both the "food" and "cocaine" levers were extended and the rats could choose between the two reinforcers. Next, rats received discrete trial tests during which both levers were extended but responses led to either cocaine or food reinforcement followed by retraction of the levers for the 20s. Finally, under the same conditions, the lever-reinforcer relation was switched during reversal tests.

**Results:** During discrimination and discrete tests, males choose food significantly more than cocaine. Whereas females displayed no significant preferences on discrimination tests but choose cocaine significantly more than food on discrete and reversal tests with estrus females choosing cocaine the most frequently.

**Conclusions:** These data indicate that selection between food and cocaine is different in males and females with females valuing cocaine more than males and estrus females showing the strongest preference for cocaine over food.

**Support:** Supported by a NARSAD grant to TEK.

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**HIGHER PSYCHIATRIC COMORBIDITY AND SEVERITY OF PROBLEMS AMONG SUBSTANCE ABUSERS WITH ADHD.**

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**Aims:** Comorbidity between substance use disorders (SUD) and attention deficit and hyperactivity disorder (ADHD) is usually associated to many problems as earlier onset of substance use, more rapid transition from use to abuse and dependence, poorer treatment adherence, more relapses and more difficulty remaining abstinent. Nevertheless, it is not clear in the literature whether or not there are other psychiatric disorders associated to this specific comorbidity and how they affect these individual's lives. This study aims at evaluating other comorbidities and the severity of problems among this population.

**Methods:** A cross-sectional multi-center sample of 285 current adult substance abusers from outpatient and inpatient clinics was collected by three research centers located in Brazilian state capitals. All subjects were evaluated with the Adult ADHD Self-report Scale (ASRS), the sixth version of the Addiction Severity Index (ASI6) and MINI-Plus. Ninety eight subjects screened positive for ADHD were compared to the negative ones (n=187).

**Results:** Individuals with comorbid SUD and ADHD showed more severe problems in ASI areas when compared to individuals without ADHD. These problems were related to drug use, unemployment as well as family and social relationships. Other psychiatric disorders such as depressive disorder, suicidal risk, manic episodes and general anxiety disorder were also higher in this population. Use of marijuana and cocaine was higher in the ADHD group even when controlled by confounding factors.

**Conclusions:** Our results suggest that comorbid SUD and ADHD is associated to more severe problems not only related to the course of the substance disorders or the amount of drug consumption but also to the social and psychiatric disabilities. This is also one of the first studies in a adult sample that demonstrate that ADHD may be a risk factor for marijuana and cocaine use.

**Support:** This study was supported by National Secretariat for Drug Policy (SENAD)

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**TRAJECTORIES OF ILLICIT DRUG USE AMONG ADULTS IN THE GENERAL POPULATION (THE CARDIA STUDY).**

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**Aims:** Research on long-term outcomes of illicit non-marijuana drug use among general population adults (i.e. not treatment samples) often relies on a single drug use measure at baseline, without assessing changes in drug use over time and with age. We used group-based trajectory modeling to explicate longitudinal patterns of non-marijuana drug use in a cohort of initially young adults assessed over a 20 year follow-up.

**Methods:** Repeated self-reports of drug use were collected in the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a cohort of 4861 healthy adults (balanced for race, gender, and education) recruited in 1985-86 at ages 18-30 and followed for 20 years. Recent cocaine, opiate, and amphetamine use (# days in the past 30) was subjected to trajectory analysis (PROC TRAJ), and differences among the resulting trajectory groups were assessed on baseline demographics, concurrent substance use, and psychosocial risk factors.

**Results:** Four distinct groups emerged: No Current Use (NO, n = 4241), Early Low Use that Declined (ELU, n = 561), Early High Use that Declined (EHU, n = 23), and Late Emerging Use (LEU, n = 36). The EHU and LEU groups were disproportionately Black and male. Baseline economic difficulties were more common in the EHU (13%) and ELU (8.6%) groups compared to the LEU (2.8%) group (p < .001). Over half of participants in all groups smoked cigarettes at baseline except for the NO group (25%), and risky alcohol use in the 15th follow-up year was more common in the EHU (38%) and LEU (40%) groups compared to the ELU (14%) and NO (2%) groups (p < .0001). The EHU and LEU groups had higher baseline anxiety, depressive, and hostility scores compared to the LEU and NO groups.

**Conclusions:** Non-marijuana drug use may peak early in life or emerge during middle age. Both patterns are associated with other risk factors. Trajectory analysis could help elucidate health and social consequences of these distinct drug use patterns in the general population.

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**USING COMMUNITY-BASED PARTICIPATORY RESEARCH TECHNIQUES TO SCREEN FOR SUBSTANCE ABUSE IN LOW-INCOME PREGNANT WOMEN RECEIVING WIC SERVICES.**

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**Aims:** Prenatal substance use is associated with adverse maternal & neonatal outcomes. Unfortunately, many pregnant women do not access prenatal care due to fears of social disapproval and legal sanctions. Alternative strategies are needed to identify pregnant women at risk for prenatal drug use, as early detection and intervention could prevent negative outcomes. We examined utility of screening for substance use in low income pregnant women attending an urban Women, Infants and Children (WIC) program. Historically, WIC sites have been hesitant to participate in research. CBPR techniques were used to foster a collaborative partnership focused on improving maternal/infant health.

**Methods:** Pregnant women at WIC sites completed a confidential interview with substance screening as part of baseline for a pilot RCT.

**Results:** To date, 50 pregnant women completed research screening (semi-structured interview with standardized quantity/frequency questions & problem-focused measures). Demographically, women were African-American (72%), never married (80%), with a mean age of 25. Mean estimated gestational age (EGA) at screening was 17 weeks. Rates of prenatal illicit drug use were comparable to national prevalence rates, with 16% of women reporting tobacco use and 18% reporting consumption of at least 4 drinks per week during the 3 months prior to pregnancy awareness. Rates of illicit drug use were substantively higher than normative data, with 18% of women reporting illicit drug use in the 6 months prior to study participation. Clinic record abstraction is nearing completion and will allow investigators to compare research prevalence rates to those obtained by WIC staff.

**Conclusions:** Findings suggest WIC programs offer a promising site for identifying pregnant women at risk for substance use. A CBPR approach was critical to study launch. Most importantly, research data will be used to inform revisions to current WIC practices, with hopes for better identification of pregnant woman at risk for substance use problems.

**Support:** Funded by VCU Institute for Women's Health grant.

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### RACIAL DIFFERENCES IN HIV DISCORDANT SEXUAL PARTNERSHIPS AND SEXUAL MIXING BETWEEN INDIVIDUALS WITH DIFFERENT SOCIAL, DRUG USE, AND SEXUAL RISK.

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**Aims:** Blacks in the United States (US) are disproportionately infected with HIV. This may be the case, in part, because sexual mixing between those with high and low risk of infection is more common among blacks than non-blacks. Identifying the type of sexual mixing that is disproportionately common among blacks—mixing by socio-demographic characteristics, drug use, or sexual risk—may improve HIV prevention efforts and our understanding of the factors driving the racial disparity in infection.

The aim of this study was to conduct a dyadic analysis to compare sexual mixing levels within black versus Latino couples.

**Methods:** We conducted a social network study in a minority population recruited in Bushwick, Brooklyn, NY, an area with high levels of poverty and substance use. We compared the prevalence of differences in biologically-confirmed HIV and HIV risk factors in 42 black versus 201 Latino sexual partnerships.

**Results:** HIV prevalence was much higher among blacks (22%) than Latinos (8%). HIV discordance was higher in partnerships between black respondents (22% of partnerships) than Latino respondents (11%). It appeared that in higher proportions of black couples versus Latino couples, partners differed in age by five years or more (57% versus 48% of partnerships), history of crack use (44% versus 27%), and history of incarceration (57% versus 49%). Injection drug use discordance was more common in Latino couples (34%) than black couples (24%). Levels of multiple partnerships, group sex involvement, and sex trade were comparable in black and Latino couples.

**Conclusions:** Sexual mixing between partners who differ in age, crack use, and incarceration history was more common within black than Latino couples. Differential sexual mixing by these attributes may contribute to disproportionate HIV infection among blacks and warrants further study.

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### 3,4-METHYLENEDIOXYMETHAMPHETAMINE DECREASES PLASMA ASYMMETRIC DIMETHYLARGININE: A PLACEBO-CONTROLLED STUDY IN HUMANS.

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**Aims:** Hyponatremia is an infrequent but severe complication of MDMA (3,4-Methylenedioxyamphetamine, 'Ecstasy') abuse, which may be mediated by increases in arginine vasopressin (AVP) secretion. AVP effects on water reabsorption may be partly mediated by neuronal nitric oxide synthase (NOS) since infusion of the endogenous NOS inhibitor asymmetric dimethylarginine (ADMA) produces renal sodium retention. ADMA may act by stimulating relocation of aquaporin 2 (AQP2) from cytoplasmic vesicles to the plasma membrane. We hypothesized that MDMA would decrease ADMA.

**Methods:** In this double-blind, within-subject placebo-controlled study, plasma or serum levels of ADMA, symmetric dimethylarginine, AVP, arginine and sodium were measured in ten healthy MDMA-experienced volunteers who received a single oral dose of MDMA (1.5 mg/kg). Data were analyzed by ANOVA.

**Results:** MDMA decreased ADMA from  $0.55 \pm 0.12$  (mean  $\pm$  SD)  $\mu\text{mol/L}$  to  $0.47 \pm 0.079$   $\mu\text{mol/L}$  ( $p < 0.05$ ) and Arginine from  $111.05 \pm 32.25$   $\mu\text{mol/L}$  to  $86.75 \pm 19.37$   $\mu\text{mol/L}$ , ( $p < 0.0001$ ) while symmetric dimethylarginine, AVP, sodium and creatinine remained unchanged.

**Conclusions:** Decreases of the endogenous NOS inhibitor ADMA, acting through AQP2, may contribute to the risk of developing hyponatremia in MDMA abusers. However, a single 1.5 mg/kg MDMA dose did not alter serum sodium, suggesting additional factors (e.g., higher or more frequent MDMA doses, excessive fluid intake, individual vulnerability) are important for developing MDMA-related hyponatremia.

**Support:** NIH DA 017716, DA 016776, and RR-00079

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### MENTAL HEALTH OUTCOMES AND DRUG USE TRAJECTORIES AMONG ADULTS IN THE GENERAL POPULATION (THE CARDIA STUDY).

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**Aims:** Prospective studies of long-term mental health outcomes of illicit drug use among general population adults are uncommon, and may fail to account for changes in drug use. We used group-based trajectory modeling to study changes in depressive symptoms and handling of anger (anger-in expression) in relation to non-marijuana drug use among general population adults.

**Methods:** Repeated measures of drug use were collected in the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a cohort of 4861 healthy adults (balanced for race, gender, and education) recruited in 1985-6 at age 18-30 and followed for 20 years. Intensity of recent cocaine, opiate and amphetamine use (number of days in the last 30) was subject to trajectory analysis (SAS PROC TRAJ). We assessed whether resulting trajectory groups differed in 15-year change in depressive symptoms (CES-D) and anger-in expression, controlling for demographics and psychiatric diagnosis at baseline.

**Results:** Four trajectory groups emerged: No Current Use (NO,  $n = 4241$ ), Early Low Use that Declined (ELU,  $n = 561$ ), Late Emerging Use (LEU,  $n = 36$ ), and Early High Use that Declined (EHU,  $n = 23$ ). Depressive symptoms at Years 5/20 were higher in groups with more intensive adult drug use (mean CES-D for ELU =  $12.2/11.3$ ; LEU =  $13.8/13.6$ ; EHU =  $17.8/14.7$ , NO =  $11/8.9$ ) ( $p < 0.001$ ). However, the LEU group was unique in not experiencing a decline in depressive symptoms from year 5 to year 20 (CES-D change for LEU =  $+0.17$  vs.  $-1.91$ ,  $-0.55$ , and  $-3.21$  for NO, ELU and EHU, respectively,  $p = .02$  for group comparison in adjusted analyses). Anger-in scores (and change in anger-in scores) did not differ between drug use trajectory groups.

**Conclusions:** Nonmarijuana drug use is associated with more depressive symptoms. While such symptoms declined for most adults in this large community-based sample, no decline occurred for persons with late-emerging drug use.

**Support:** NIDA R01-DA-025067; NHLBI N01-HC-95095

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### BEHAVIORAL-STIMULANT AND NEUROCHEMICAL EFFECTS OF MONOAMINE RELEASERS WITH VARYING SELECTIVITY FOR DOPAMINE AND SEROTONIN IN SQUIRREL MONKEYS.

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**Aims:** The development of an effective medication to treat psychostimulant abuse remains elusive. Amphetamine, which acts as both a dopamine transporter inhibitor and a dopamine releaser, reduces cocaine self-administration in both animals and humans. However, amphetamine is itself a drug of abuse, limiting its utility as a medication. The amphetamine analogs PAL-353, PAL-313, and PAL-287 exhibit a ratio for releasing dopamine vs. serotonin as follows: 0.01, 0.83, and 3.7, respectively. In comparison, amphetamine has a ratio of 0.004, while the selective serotonin releaser fenfluramine has a ratio of 126. The purpose of the current study was to evaluate the stimulant effects of these drugs on operant behavior maintained by a fixed-interval schedule in squirrel monkeys.

**Methods:** Behavioral effects were compared with changes in extracellular dopamine measured with in vivo microdialysis in the nucleus accumbens of a separate group of squirrel monkeys.

**Results:** Both amphetamine (0.03-1.0 mg/kg) and PAL-353 (0.03-1.7 mg/kg) induced stimulant effects in a dose-dependent manner, with a peak effect at 0.3 mg/kg. In contrast, PAL-313 (0.3-1.7 mg/kg), PAL-287 (0.03-3.0 mg/kg), and fenfluramine (0.3-3.0 mg/kg) only decreased operant behavior. Although amphetamine, PAL-353, and PAL-287 all increased dopamine levels in the nucleus accumbens, this increase was greater following amphetamine and PAL-353 than following PAL-287. Notably, PAL-287 induced robust increases in dopamine in the absence of behavioral-stimulant effects.

**Conclusions:** Therefore, the increased selectivity for serotonin not only blunted the presynaptic release of dopamine but also the stimulant effects of dopamine release on operant behavior.

**Support:** Supported by USPHS grants DA00517 (LLH), DA10344 (LLH), DA12970 (BEB), and RR00165.



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### CHANGES IN HPA AXIS FUNCTION AND PSYCHIATRIC SYMPTOMS IN ADOLESCENT METHAMPHETAMINE USERS.

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**Aims:** Methamphetamine (METH) is a widely abused psychostimulant that induces neurotoxicity and neurocognitive impairments in adults. However, the effects of METH use in adolescents are unclear because of limited research. The current experiments examined HPA axis and neurocognitive function in adolescent METH users.

**Methods:** Subjects were METH users and non-drug user controls between the ages of 12 and 23 years. All subjects were given the Symptom Check List 90 and Brief Psychiatric Rating Scale to assess psychiatric symptoms. Lastly, the subjects took the Trier Social Stress Test, and salivary cortisol levels measured.

**Results:** There were no significant differences between the METH users and control subjects in age or education. There were no significant differences between male and female METH users in METH use characteristics such as age of first use, amount and frequency of usage, or lifetime exposure. METH users exhibited significantly more manic and depressive symptoms than controls on the BBRS. Male METH users had a higher basal cortisol level than male controls, while female METH users exhibited significantly larger cortisol response to the TSST than female controls, as well as higher scores on the Positive Symptom Distress Index of the SCL 90 than female control subjects. Cortisol AUC curves were significantly correlated with both the depressive index and Positive Symptom Distress Index scale of the SCL90. Lifetime METH exposure also correlated with basal cortisol levels.

**Conclusions:** Overall, METH use appears to induce significant psychiatric symptoms in adolescents. In addition, Female METH users may be more stressed than female controls, and that this may contribute to the psychiatric sequelae seen in these subjects.

**Support:** The study was supported by the NIH [2U54 NS3906 and 1U54 NS056883 (Specialized Neuroscience Research Programs), K24 DA016170 (LC); K02 DA016991 (TE), K01 DA 021203 (CC); The National Center for Research Resources G12RR003061-21 (RCMI) and 5P20 RR11091-10 (RCMI-CRC)].

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### ANATOMICAL AND FUNCTIONAL INTERACTIONS BETWEEN CHEMOKINE AND $\mu$ -OPIOID RECEPTORS IN PERIAQUEDUCTAL GREY NEURONS.

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**Aims:** Opioids have immunomodulatory functions and may alter susceptibility to immune disorders. Conversely, behavioral studies have shown that chemokines, a family immunomodulatory molecules, block opioid analgesia within the periaqueductal grey (PAG). The purpose of this study was to investigate the anatomical relationship and functional interactions between  $\mu$ -opioid receptors (MOR) and two chemokine receptors in the rat brain: CXCR4 and CX3CR1 whose chemokine ligands are stromal cell-derived factor-1 $\alpha$  (SDF-1 $\alpha$ ) and fractalkine, respectively.

**Methods:** We employed immunohistochemical techniques to investigate MOR/CXCR4 and MOR/CX3CR1 receptor colocalization in multiple brain regions. To test functional receptor interactions in the PAG, we examined the effect of the  $\mu$ -opioid morphine or a chemokine (SDF-1 $\alpha$  or fractalkine) alone or in combination on membrane properties of PAG neurons using whole-cell patch-clamp recordings in rat brain slices.

**Results:** Our results demonstrate co-expression of each chemokine receptor with MOR on individual neurons in several brain regions including PAG, hippocampus and cingulate cortex. Electrophysiology studies show that morphine (10  $\mu$ M) produced a membrane hyperpolarization coupled with a decrease in input resistance in PAG neurons. SDF-1 $\alpha$  or fractalkine (10 nM) alone had no electrophysiological effect. However, in the presence of SDF-1 $\alpha$ , morphine's electrophysiological effects were blocked in all PAG neurons tested. In the presence of fractalkine, morphine's effects were blocked in 60% of the PAG neurons tested.

**Conclusions:** These data provide electrophysiological evidence for heterologous desensitization between MOR and two chemokine receptors at the level of single neurons in PAG brain slices. These chemokine-opioid interactions may contribute to a range of clinical phenomena such as the limited utility of opioid analgesics for treatment of inflammatory pain and the well-known relationship between opiate abuse and immune disorders such as AIDS.

**Support:** Supported by DA 20126, DA 06650 and the PA Dept. of Health.

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### THE IMPACT OF GENDER AND OTHER BASELINE CHARACTERISTICS ON AIDS RISK PERCEPTION RATINGS.

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**Aims:** To assess gender differences in AIDS risk perception and behavior in order to understand issues for AIDS prevention programming to substance-dependent males and females.

**Methods:** Data were collected at baseline in association with a study of early engagement strategies for substance-dependent individuals ( $N = 655$ ; 52% male) entering drug-free outpatient treatment. Severity of drug problems was assessed using the Addiction Severity Index. Overall psychological distress (Global Severity Index [GSI]) and total number of psychological symptoms reported (Positive Symptom Total [PST]) were assessed using the SCL-90R. AIDS risk perceptions and behaviors were assessed using the TCU AIDS Risk Assessment (ARA). Principal factor analyses of the TCU ARA risk perception ratings in each gender separately supported single-factor solutions used to create an overall perception rating for each gender. Stepwise regression analyses with backward removal examined associations between baseline characteristics and the overall AIDS risk perception ratings separately by gender.

**Results:** For males, the number of sexual partners in the last 30 days ( $p=.008$ ), intravenous drug use ( $p=.016$ ), and GSI ( $p=.003$ ) were positively associated, while the number of sexual encounters in the past 30 days was negatively associated with AIDS risk perception ratings ( $p=.001$ ). For females, the ASI Drug Composite Score ( $p=.002$ ), the number of times engaging in sexual intercourse in the past 30 days ( $p=.045$ ) and PST scores ( $p=.007$ ) were positively associated, whereas GSI ( $p=.002$ ) was negatively associated with risk perception ratings.

**Conclusions:** Substance-dependent men and women entering treatment perceive their AIDS risk differently. Results suggest that different approaches towards men and women may be beneficial in addressing risky behaviors related to AIDS. Of particular concern are the significant, but differing, associations between psychological functioning and AIDS risk perception by gender.

**Support:** NIDA grant RO1 DA 11402

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### PREDICTION OF CANNABIS USE DISORDER BETWEEN CHILDHOOD AND YOUNG ADULTHOOD USING CORTISOL REACTIVITY, TRANSMISSIBLE AND NON-TRANSMISSIBLE LIABILITY INDICES.

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**Aims:** This prospective investigation evaluated whether cortisol reactivity during experimentally induced mild stress in children (age 10-12) and adolescents (age 16) mediates the association between parental SUD and offspring's transmissible liability for cannabis use disorder (age 22)

**Methods:** This prospectively tracked sample ( $n=500$ ) afforded the opportunity to explicate the etiological trajectory beginning prior to drug use to cannabis use disorder. Research conducted under the aegis of the Center for Education and Drug Abuse Research has revealed that the individual and environment components of SUD can be quantified as unidimensional interval scales. The transmissible liability index (TLI), quantifies psychological characteristics which are common to risk for the different categories of SUD in the DSM-IV. A non-transmissible liability index (NTLI) has been derived which is essentially orthogonal to the TLI, and predictive of cannabis use disorder

**Results:** Parental SUD significantly predicted TLI (age 10-12 and 16:  $b=.42$ ,  $b=.52$ ,  $p<.001$ ). The cortisol reactivity score at age 16 significantly predicted TLI (age 16:  $b=.13$ ,  $p<.05$ ) whereas cortisol (age 10-12) predicted NTEI at age 16. The indirect path from parental SUD to TLI through cortisol reactivity was not significant. In addition, TLI and NTEI at age 16 significantly predicted illicit drug use at age 19 ( $b=.28$ ,  $.17$ ,  $p<.001$ ) which in turn predicted cannabis use disorder at age 22 ( $b=.68$ ,  $p<.001$ )

**Conclusions:** The intervention between familial and environmental risk has important practical ramifications for prevention of SUD. For example, in conjunction with family history and environment context, cortisol reactivity may be an informative non-intrusive biomarker to improve estimation of SUD risk. Demonstrating that it is possible to identify youths at high risk for cannabis use disorder provides the foundation to design prevention interventions targeted at the factors associated with risk

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### MDMA REDUCES SEROTONIN TRANSPORTER CELL SURFACE EXPRESSION VIA A P38MAP KINASE INDEPENDENT MECHANISM.

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**Aims:** To determine the cellular effects of MDMA on serotonin transporter (SERT) expression

**Methods:** Male Sprague Dawley rats were administered 4 intraperitoneal injections of MDMA (10 mg/kg) every 2 hrs and sacrificed on day 14. Brain tissue was removed and total SERT protein levels determined using SDS-PAGE and quantitative Western Blotting. RNA was extracted and processed for quantitative RT-PCR. Changes in cell surface expression were determined using biotinylation and live-cell confocal microscopy techniques in human embryonic kidney and mouse neuroblastoma cells expressing green fluorescent protein tagged human SERT (GFP-SERT). Activation of p38MAP kinase (p38MAPK) was determined using antibodies recognising active phosphorylated p38MAPK.

**Results:** Our results show no change in SERT mRNA in the dorsal raphe (n=7-11), or total SERT protein from the Striatum or Nucleus Accumbens (n=7-9) in rats exposed to MDMA. In a SERT expressing cell system we show MDMA (1-10 µg/ml) results in a dose dependent and rapid increase in internalized SERT protein compared to vehicle treated controls (n=23). Both cell-surface biotinylation and live-cell confocal experiments show that MDMA results in down-regulation within 5 min. This effect is sustained for at least 90 min. UV light exposure, consistently gave an intense band of phospho-p38MAPK compared to controls (p<0.001). However, there was no significant difference between MDMA and vehicle treated cells (n=15). All statistical analysis consisted of one-way ANOVA followed by Bonferroni's Multiple Comparison Test. A value of p<0.05 was deemed to be statistically significant.

**Conclusions:** No change in total SERT protein or mRNA was seen in rats administered MDMA. Results from cellular studies show rapid redistribution of SERT from cell surface to intracellular vesicles. This redistribution was found to be via a p38MAPK independent mechanism.

**Support:** The Neurological Foundation of New Zealand, The Laura Trask Foundation, Wellington Medical Research Foundation and Victoria University of Wellington.

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### SEXUAL ORIENTATION, DRUG USE DURING SEX, AND HIV RISK PRACTICES/PREFERENCES AMONG MEN WHO USE THE INTERNET TO FIND MEN FOR UNPROTECTED SEX.

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**Aims:** Recent evidence has shown that, increasingly, men looking for risky sex are turning to the internet to find sex partners. This paper examines the interplay of sexual orientation, engaging in drug use during sex, & HIV risk practices/preferences in a population of men who use the internet to find men for unprotected sex.

**Methods:** This study is based on a content analysis of 1,434 profiles, randomly selected based on ZIP code, posted on 1 internet website specifically promoting unprotected sex among men. Data were collected from 9/06-9/07. Risk practices & risk preferences of 1,300 gay/bisexual men are compared to 134 self-identified heterosexual/curious men. Risk behaviors, risk preferences, & preference for drug use during sex (PNP) were all coded based on info contained in each profile.

**Results:** 53% of the men expressed a desire for PNP. Gay/bisexual men who sought PNP partners had profiles indicating the greatest desire for risky sex and sexual preferences that heightened overall risk levels. Compared to the other groups, they were more likely to: want multiple partner sex (p<.0001), engage in felching (p<.0001), accept semen orally/analytically (p<.0001), state a distaste for condoms (p<.004), want anonymous sex (p<.03), & indicate that they do not care about partners' HIV status (p<.0001). Second ranked in terms of risk were gay/bisexual men who did not seek PNP partners, followed by heterosexual/curious men who wanted to find PNP partners, & then heterosexual/curious men who did not want to find PNP partners.

**Conclusions:** Seeking partners with whom one can engage in sex while high was commonplace among men using the internet to find partners for unprotected sex. Gay/bisexual men who looked for PNP partners were at the greatest risk for contracting/transmitting HIV; they are a group needing targeted intervention efforts. It should be borne in mind that even the lowest-risk group studied—heterosexual/curious men who were not looking for PNP partners—is at great risk for contracting HIV, because they are using a website specifically promoting unsafe sex.

**Support:** NIDA

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### RELATIONSHIP OF IMPULSIVITY AND DECISION-MAKING MEASURES IN COCAINE DEPENDENCE.

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**Aims:** Compare cocaine dependent subjects to controls on a measure of decision-making (Iowa Gambling Task or IGT) and its parameters extrapolated by cognitive modeling, a questionnaire measure of impulsivity (Barratt Impulsiveness Scale or BIS-11) and a measure of behavioral inhibition (immediate memory task or IMT), and examine the relationship between measures of decision-making, behavioral inhibition and impulsivity.

**Methods:** Methods: A total of 66 treatment seeking cocaine dependent subjects and 20 healthy control subjects were screened for inclusion with physical exam and structured psychiatric interview. Cocaine dependent subjects were excluded if they did not meet DSM-IV criteria for current cocaine dependence and reported recent cocaine use (a majority with cocaine positive urines), had Axis I disorder other than substance induced mood disorder, or with evidence of general medical condition. Healthy controls were excluded for the same criteria plus current or past substance abuse or dependence. BIS-11, IMT, and IGT were administered to subjects and controls. Cognitive model analysis using the Expectancy-Valence Model (Busemeyer & Stout, 2002) was applied to results from IGT, which assesses parameters of decision-making into consistency, attention, and learning/memory.

**Results:** Results: Cocaine dependent subjects had significantly higher scores on the BIS, more commission errors on the IMT, and more disadvantageous choices on the IGT. There was a significant correlation between BIS scores and IMT commission errors, but there was no significant correlation between IGT total score and IMT or BIS-11 (p= .280, r= -.127 and p= .174, r= -.148 respectively). No correlation was seen between cognitive model parameters and IMT false alarms or BIS-11 total score.

**Conclusions:** Conclusion: While impulsivity and decision-making are both cognitive processes seen affected by cocaine use and dependence, measures of impulsivity and decision-making measure different cognitive processes in these individuals.

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### COGNITIVE PERFORMANCE AND METHADONE MAINTENANCE PATIENTS.

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**Aims:** The aim of this study was to examine cognitive performance in methadone patients (MP) being maintained on different dose levels (lower dose group, LDG: ≤ 85 mg/day; higher dose group, HDG: ≥ 110 mg/day) in community clinics before and after methadone dosing.

**Methods:** During two sessions, MP received double-blind administration of an oral solution 120 min before, and immediately after, a performance assessment battery. During the acute methadone session, the pre-battery solution contained the MP's usual methadone dose and the post-battery solution contained placebo. During the placebo session, the pre-battery solution contained placebo and the post-battery solution contained methadone. Mean maintenance dose was 67.7 mg in the LDG (N = 15) and 133.2 mg in the HDG (N = 14).

**Results:** A 2 X 2 Analysis of Variance was carried out with acute dose (placebo/methadone) and maintenance dose group (lower/higher) as factors. Main effects of acute dose revealed that methadone significantly decreased overall arousal (flicker fusion) and slowed reaction time on working memory (modified Sternberg task) and divided attention tasks (p < .05). Main effects of maintenance dose revealed that individuals in the HDG had slower reaction time and decreased accuracy on the divided attention task relative to the LDG (p < .05). Significant interactions were observed such that tracking moves on the divided attention task were slowed by acute methadone dosing in the HDG but not the LDG, and working memory accuracy (modified Sternberg) was impaired by acute methadone dosing in the LDG but not the HDG (p < .05). Several outcomes were not altered by acute or maintenance dose: psychomotor function (DSST), episodic memory (free recall), and an additional measure of working memory (n-back).

**Conclusions:** These results suggest that cognitive performance may be slowed following daily methadone dosing relative to before dosing, and that more cognitive slowing occurs in MMP being maintained on higher doses.

**Support:** This work was supported by NIDA grant DA17688, DA023186, T32DA07209.

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**ANTIRETROVIRAL USE AMONG HIV+ INJECTION DRUG USERS: THE ROLE OF METHADONE MAINTENANCE AND PROVIDER ENGAGEMENT.**

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**Aims:** Injection drug users (IDUs) are at disproportionate risk of HIV and have low access to antiretroviral therapy (ART), contributing to HIV health disparities. IDUs often have difficulty engaging in medical care and accessing methadone treatment. This study sought to identify structural, interpersonal and individual-level factors associated with IDUs' ART use. Finding will inform multi-level, contextually-tailored intervention to improve this population's access to HIV treatment.

**Methods:** Cross-sectional data from 3 semi-annual assessments were combined, and logistic regression with the GEE method was used. Participants were a community sample of HIV+, active IDUs enrolled in the INSPIRE study, a multisite prevention intervention. The baseline sample (n=1,161) comprised 75% current drug users, 63% males, and 60% with a CD4 count <350. At baseline, 55% reported taking ART, which did not significantly differ at 6- and 12-months follow-ups.

**Results:** Adjusted analyses indicated that IDUs' ART use was independently associated with structural factors of methadone treatment, stable housing, frequency of medical visits, and medical coverage; the interpersonal factor of patient-provider engagement; and individual-level factors of lower depressive symptoms, male sex, and a positive attitude about ART benefits to health even if using illicit drugs.

**Conclusions:** The findings suggest that interventions to improve IDUs' HIV treatment and reduce their HIV health disparities ought to promote IDUs' access to integrated medical and drug abuse treatment services, relationship-focused patient-provider interactions, and stable housing. Clinician and IDU training on patient-provider interaction and substance abuse as a chronic condition necessitating ongoing treatment services may facilitate IDUs' engagement in care and reduce their disparities in HIV health outcomes. Particular attention is needed to ensure women IDUs' access to HAART.

**Support:** CDC & HRSA

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**GENDER DIFFERENCES IN PATTERNS OF ALCOHOL DEPENDENCE SYMPTOMS: EVIDENCE FROM A LATENT EMPIRICAL APPROACH.**

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**Aims:** To understand the variation in response to alcohol with respect to dependence symptoms, and to describe associations of these groups with demographic characteristics, including gender, and treatment.

**Methods:** Data from combined 2002-2005 public use National Survey on Drug Use and Health identified 110,742 past-year alcohol users aged 18 years or older. Latent class analysis was used to define classes based on observed clustering of DSM-IV alcohol dependence symptoms. Multivariate latent class regressions were used to compare gender, other sociodemographic characteristics, and treatment across these classes.

**Results:** The four-class model had the best fit and identified classes that differed quantitatively and qualitatively, with 2.3% of the users in Class 2 (most severe) and 83.8% in Class 1 (not affected). Heterogeneity in patterns of alcohol abuse symptoms was observed; 20% of the most severe class did not have any alcohol abuse symptoms. These profiles differed by a number of sociodemographic characteristics, including gender. Male past-year alcohol users were twice more likely to be in the moderate and most severe classes than in non-symptomatic class. Across classes, males were approximately 1.4 to 2 times more likely to report perceived need for and received treatment than their female counterparts. Overall, approximately 19% of the most severe class and less than 5% of the moderate/subthreshold classes received treatment for alcohol in the past year.

**Conclusions:** The overall percentage of individuals receiving treatment was low. Although males were more likely to be in the affected classes than in the non-affected class compared to females, there is a great disparity in receiving treatment among women. This disparity should be further investigated longitudinally.

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**SMOKING CESSATION SERVICES IN DRUG ABUSE TREATMENT: A NATIONAL STUDY.**

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**Aims:** Given that the majority of individuals receiving drug treatment also smoke cigarettes, the delivery of smoking cessation services in these treatment settings has high public health significance. Few studies have examined this aspect of treatment service delivery. The aim of this study is to estimate the associations between organizational characteristics and the adoption of smoking cessation services in drug abuse treatment organizations.

**Methods:** Telephone interviews were conducted with administrators of 618 drug abuse treatment organizations. Data were used to construct a typology of smoking cessation services, including counseling-only services, medication-only services, and comprehensive services (counseling and pharmacotherapy). Organizational characteristics and prior adoption of two smoking cessation-related measures (teaching smoking cessation techniques to patients and use of medications) were extracted from a previous dataset. Multiple imputation and multinomial logistic regression was used to analyze the data.

**Results:** The majority (53.6%) of organizations offered no smoking cessation services. About 6.0% offered counseling-only, 27.5% offered medication-only, and 12.9% offered comprehensive smoking cessation services. Organizational characteristics associated with the availability of medication-only and comprehensive services included reliance on governmental funding, location in a hospital, availability of more intensive levels of care, organizational size, and access to physicians. Notably, these associations were significant when prior adoption was controlled. Organizational characteristics were not associated with counseling-only services.

**Conclusions:** Although most had not adopted these services, certain types of organizations were more likely to adopt smoking cessation services. Programs based in hospitals, with more intensive levels of care, and with access to physicians were more likely to adopt pharmacological approaches to smoking cessation.

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**EFFECTIVENESS OF COCAINE ESTERASES AGAINST CARDIOVASCULAR TOXICITY AND LETHALITY PRODUCED BY INTRAVENOUS ADMINISTRATION OF COCAINE IN RATS.**

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**Aims:** A bacterial cocaine esterase (CocE) is the most efficient native enzyme for metabolizing cocaine. However, CocE has a relatively short half-life of 10 minutes in vivo. A recent study has identified a thermostable CocE mutant, T172R-G173Q, which has a ~30-fold increase in plasma half-life both in vitro and in vivo (Gao et al., Mol. Pharmacol. DOI:10.1124/mol.108.049486). The aim of this study was to investigate the in vivo potency of the wild-type CocE and T172R-G173Q in blocking intravenous cocaine-induced toxicity in rats.

**Methods:** Cocaine toxicity was quantified by measuring the cardiovascular changes and the occurrence of convulsions and lethality.

**Results:** Intravenous cocaine (1-6 mg/kg) produced a dose-dependent increase in both PQ and QRS intervals in freely moving rats implanted with radio-telemetric probes (DSI, TA10 CTA-F40). Pretreatment with both enzymes (0.1-1 mg/kg) dose-dependently eliminated intravenous cocaine 3 mg/kg-induced prolongation of the QRS interval. In addition, intravenous cocaine 10 mg/kg produced convulsions in all tested rats and subsequent death in 80% of tested rats. This dosing condition of intravenous cocaine 10 mg/kg was chosen to test the ability of enzymes to rescue convulsing rats. Intravenous administration of wild-type CocE or T172R-G173Q (0.1-1 mg/kg), given 1 min after the occurrence of intravenous cocaine-induced convulsions, shortened the recovery time from convulsions and save all rats from subsequent death. More importantly, both enzymes are equally potent in reversing cocaine toxicity.

**Conclusions:** Taken together, a newly identified long-acting CocE mutant, T172R-G173Q, produces robust effects to prevent and reverse cocaine toxicity in rats. The improved thermostability of CocE mutants will have a profound impact on their therapeutic potential for the treatment of cocaine overdose and addictions in humans.

**Support:** This study was supported by US Public Health Service Grants DA-023213 and DA-021416.

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**THE REGULATION OF CRAVING FOR CIGARETTES VS. FOOD: AN FMRI STUDY OF CIGARETTE SMOKERS.**

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**Aims:** A failure to regulate craving has been implicated in substance use disorders, underscoring the need to understand the neural correlates of craving and its regulation in substance abusing populations. Therefore, this study used fMRI to examine the neural correlates of the regulation of craving using cognitive strategies in tobacco cigarette smokers.

**Methods:** Twenty-one cigarette smokers were scanned as they viewed images of cigarettes and appetizing food, and were instructed to think about either the (a) immediate sensory experience (e.g. "increase craving" trials), or (b) the long-term negative physical health consequences associated with consuming each item (e.g. "regulate craving" trials). After each trial, participants indicated their level of craving for each item.

**Results:** Participants reported significantly less craving for both cigarettes and food on "regulate craving" trials, suggesting that cognitive strategies can be used to effectively decrease craving for both food and cigarettes. This is consistent with clinical data. Further, on "increase craving" compared to "regulate craving" trials, activations were observed in "reward" regions including subgenual cingulate, ventral striatum, and ventral tegmental area. This pattern was stronger for cigarettes compared to food, consistent with participants' reports of greater craving for cigarettes compared to food. Conversely, during "regulate craving" trials, activity was observed in cognitive control regions including the dorsomedial prefrontal cortex and inferior frontal gyrus. This pattern was stronger for food compared to cigarettes.

**Conclusions:** These data show that both subjective reports and neural activity associated with cravings are attenuated by cognitive strategies. Further, observed differences in neural activity between cigarettes and food suggest a possible mechanism for the impaired regulation of cigarette craving exhibited by some cigarette smokers in the natural ecology.

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**ACCESS TO A NONDRUG ALTERNATIVE REINFORCER PRODUCES A RIGHT-WARD SHIFT IN THE COCAINE DISCRIMINATIVE STIMULUS.**

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**Aims:** The environment has been shown to play an important role in drug taking. When other nondrug reinforcers are present, studies have shown that acquisition, maintenance and relapse to drug self-administration are decreased or abolished and their removal increases drug intake. The present study assessed whether access to a sweet solution could change the sensitivity to cocaine using a drug discrimination procedure.

**Methods:** Adult, male, Long-Evans rats (n=10) were initially trained to discriminate 10 mg/kg cocaine, IP from saline injections. Following acquisition, rats were tested with varying doses of cocaine (0-17.8 mg/kg in a cumulative dosing procedure) for 12 consecutive days. The 12 test days consisted of three 4-day cycles. The first cycle established a baseline of responding. During the second cycle, rats were given access to a bottle containing either a glucose (3.0%)/saccharin (0.125%) solution (G+S) or distilled water (dH2O) in addition to their ad libitum home-cage bottle. During the final cycle, the G+S/dH2O bottle was removed.

**Results:** Data were pooled for the 4 days of each cycle for a single mean ED50 [with 95% confidence interval (CI)]. The first cycle did not differ (as evidenced by overlapping CIs) between Groups pre-G+S [3.42 (2.85-3.99)] and pre-dH2O [3.08 (2.96-3.21)]. When the second bottle was presented, animals that received G+S had significantly higher ED50s [5.48 (4.87-6.08)] than their own baseline and the ED50s of animals that received dH2O [2.99 (2.71-3.28)]; which also were not different from their own baseline. During the final cycle, when the bottle was removed, ED50 values again did not differ from baseline for Group dH2O [3.38 (2.72-4.03)], but the G+S group remained higher than its baseline and the dH2O group [5.23 (4.51-5.96)]. Rate of responding was not affected throughout.

**Conclusions:** Access to a nondrug reinforcer shifted the dose-response curve for cocaine rightward, suggesting that rats were less sensitive to the cocaine cue when a sweet solution was available on the home-cage.

**Support:** This work was supported by a Mellon Foundation grant to ALR.

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**GHB- AND BACLOFEN-INDUCED HYPOTHERMIA IN MICE: INTERACTIONS WITH THE GABA-B RECEPTOR POSITIVE MODULATOR CGP7930, THE GABA-B RECEPTOR ANTAGONIST CGP35348, AND THE NOS INHIBITOR L-NAME.**

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**Aims:** GABA-B receptor activation can be modulated by drugs acting at sites other than the receptor. Such modulation offers the possibility to develop more selective treatments of disorders in which GABA-B receptors are implicated, including drug dependence. CGP7930, a positive modulator of GABA-B receptors, enhances the sedative and hypnotic effects of baclofen and gamma-hydroxybutyrate (GHB) in mice (Carai et al., EJP 504:213, 2004). The present study examined the generality of CGP7930's ability to enhance in vivo effects of GABA-B receptor agonists.

**Methods:** Body temperature was measured immediately before and 15 - 120 min after i.p. drug administration, in male C57BL/6J mice.

**Results:** Baclofen and GHB both produced hypothermia (ED50: 4.8 and 270 mg/kg, respectively). When given alone, CGP7930 also produced hypothermia, but was less potent (ED50: 100 mg/kg) and less effective than baclofen. CGP7930-induced hypothermia was not attenuated by the GABA-B receptor antagonist CGP35348, which blocked baclofen-induced hypothermia. CGP7930 did not enhance the hypothermic effects of baclofen or GHB. In contrast, the NOS inhibitor L-NAME had no effect on body temperature when given alone but enhanced baclofen- and GHB-induced hypothermia.

**Conclusions:** The finding that CGP7930 produced hypothermia when given alone, and that this effect was not attenuated by CGP35348, suggest that, in vivo, CGP7930 may behave as an allosteric agonist at GABA-B receptors. However, the results do not provide evidence that CGP7930 also behaves as a positive modulator at GABA-B receptors mediating baclofen- and GHB-induced hypothermia. Together with previous findings, the present results confirm the utility of CGP7930 for examining the role of GABA-B receptor modulation in the in vivo effects of GABA-B receptor agonists.

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**CONTINGENCY MANAGEMENT FOR SMOKING CESSATION IN ADULTS WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

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**Aims:** Individuals with ADHD smoke at higher rates than the general population and several studies have reported that smokers with ADHD have a harder time quitting. We evaluated the effects of a contingency management approach for promoting abstinence in adult smokers with and without ADHD across a two-week period.

**Methods:** In this ongoing study, 28 subjects (n=14 each with and without ADHD) have enrolled in a study to examine the effects of prolonged abstinence (up to 2 weeks) in smokers with and without ADHD. Following screening and baseline sessions, non-treatment-seeking smokers began a 2-week CM program that was implemented to promote abstinence. Subjects reported to the laboratory each day for 2 weeks and self-reported smoking and exhaled air CO levels were measured, along with a range of other measures of nicotine withdrawal, craving, and cognitive functioning. Baseline characteristics were evaluated as predictors of outcome.

**Results:** Smokers both with and without ADHD remained abstinent at high rates throughout the course of the experiment. Ten of fourteen smokers with ADHD (71.4%) and 9/14 smokers without ADHD (64.3%) remained abstinent for 2 weeks. Moreover, following the removal of the contingencies, a substantial minority of smokers in both groups who had remained abstinent stayed smoke-free for up to 10 days. Risk taking behavior at baseline was associated with sustained abstinence during the CM phase.

**Conclusions:** These findings indicate that interventions with highly salient consequences can be effective for reducing smoking in individuals with ADHD. Interventions that parametrically manipulate the contingencies would be useful for determining the optimal threshold for maintaining abstinence in smokers with and without ADHD. Also, studying the efficacy of CM in combination with other interventions (e.g., nicotine replacement therapy) or in treatment-seeking individuals would be useful.

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### THE ROLE OF SOCIAL CONTEXT IN THE RELATIONSHIP BETWEEN DRUG USE AND RISKY SEXUAL BEHAVIOR AMONG INDIVIDUALS WHO USE BOTH HEROIN AND CRACK/COCAINE.

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**Aims:** Due to an association with elevated RSB, crack/cocaine has been shown to be an important risk factor for HIV infection. The question is whether the crack cocaine-sex association is primarily pharmacological or sociocultural in nature.

The present study aimed to provide preliminary data regarding the role of sociocultural factors in the relationship between crack cocaine and risky sex.

**Methods:** We compared the context of cocaine and heroin use among 51 inner-city drug users who reported using both crack/cocaine and heroin, 4-5 times/week during the past year. Specifically, for each drug we assessed the frequency of use with others vs. alone, the frequency of use by/with one's social network, and participants' self-reported sexual functioning in the context of using each drug.

**Results:** Within subjects comparisons revealed that compared to heroin, crack cocaine is more frequently used in a social context. Furthermore, although participants did not differ in the extent to which they used heroin vs. cocaine with family, friends and neighbors, cocaine was more frequently used with a romantic partner than heroin. To further explore whether this relation may indeed reflect the pharmacological effects of crack cocaine, we compared participants' self-reported sexual desire and ability while intoxicated with crack cocaine vs. heroin. Our results speak against the pharmacological hypothesis as our participants reported a significant decrease in their sexual desire and ability while intoxicated with cocaine compared to heroin and while intoxicated with any of the drug compared to their sexual ability and desire when sober.

**Conclusions:** Our results suggest that in addition to the pharmacological dimension, the relationship between crack cocaine and sex may have an important sociocultural dimension calling for further research to explore the specifics of such dimension.

**Support:** NIDA R01 DA19405 (PI: Lejuez)

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### NEONATAL ISOLATION ALTERS MOTHER-PUP INTERACTIONS.

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**Aims:** We showed that neonatal isolation (NI) enhances cocaine self-administration and striatal dopamine levels in response to psychostimulants. Also, studies link maternal care, which is altered after a dam is separated from the pups, to neural and epigenetic changes in the offspring. Individual differences in maternal care associate with dopamine levels in ventral striatum. Thus, we sought to determine if NI (1-hr isolation/day from dam, litter, nest on PND2-9) alters maternal care after dam and litter reunite (Experiment 1). We then investigated if dams with NI experience as pups showed differential maternal care to their litters depending upon whether their litters were NI (Experiment 2).

**Methods:** In Experiment 1, 8 litters were assigned to 1 of 3 conditions: NI, handled (H; 5-min separation of dam from litter), or non-handled (NH; no separation). On PND2-9, dams were transported in the home cage to a test room for videotaping 1-hr before cessation of NI or handling or, in the case of non-handling, with their litters. Sessions (60-min) began once pups were returned to the cage and tapes were later rated blind to condition. In Experiment 2, 10-11 litters of female rats with or without NI experience were assigned to either the NI or NH litter condition.

**Results:** Results from Experiment 1 showed that dams of NI and H litters spent more time licking pups than dams of NH litters and less time picking up pups to put outside the nest. Further, non-maternal behaviors of burrowing and grooming were less in dams of NI and H vs NH litters. Some effects were greater in dams of NI vs H litters. In Experiment 2, NI-experienced dams with NI litters did not increase pup licking and failed to decrease non-maternal behaviors as seen in Experiment 1. Further, NI-experienced dams picked up pups more than NH-experienced dams in contrast to results from Experiment 1.

**Conclusions:** NI alters maternal behavior which, in turn, may shape neurobehavioral responses of the adult including effects on maternal care. NI may have epigenetic effects due to changes in maternal care that, in turn, affect neurobehavioral responses to psychostimulants.

**Support:** DA020117; U01AA013476

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### SUBSTANCE USE AND THE QUALITY OF PATIENT-PROVIDER COMMUNICATION IN HIV CLINICS.

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**Aims:** To compare the quality of communication among HIV-infected patients with and without substance use. We hypothesize patients reporting substance use may have less favorable provider-provider communication.

**Methods:** Audio-recorded encounters with 414 HIV-infected patients and 44 providers in 4 HIV clinics in the Enhancing Communication and HIV Outcomes (ECHO) study were coded using Roter Interaction Analysis System. Patients were surveyed about substance use and provider communication quality. Analysis assessed associations between substance use and dependent variables (observed provider communication behaviors, dialogue duration, and patient-rated communication quality) using GEE, adjusting for patient and provider covariates and site with provider as random effect.

**Results:** Patients reported current (29%) and former (47%) illicit drug use and current (10%) and former (49%) problem drinking. Optimal provider communication was lower among patients with current (18%,  $p=.002$ ) and past (25%,  $p<.001$ ) vs. no problem drinking (47%), but similar by those with current (36%,  $p=.661$ ) and past (29%,  $p=.116$ ) vs. no illicit drug use (38%). Dialogue duration was shorter for those with current (22min,  $p=.025$ ) and former (23min,  $p=.001$ ) vs. no problem drinking (27min). In multivariate models, provider made more critical statements to patients with current drug use vs. non-users ( $\beta=1.01$ ,  $p=.004$ ) and made fewer legitimizing statements to those with current vs. no problem drinking ( $\beta=-1.97$ ,  $p=.026$ ). Patient-rated provider communication quality remained lower for patients with current ( $\beta=-1.53$ ,  $p=.003$ ) and former ( $\beta=1.24$ ,  $p<.001$ ) vs. no problem drinking.

**Conclusions:** Both patient-rated and observed measures of patient-provider communication are lower in patients with problem drinking compared with non-users. Interventions that improve patient-provider communication in HIV treatment settings may have the greatest benefit in patients with problematic alcohol use.

**Support:** NIDA (1K23DA019808), AHRQ (8303-49316-0)

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### THE DAY TREATMENT MODALITY APPLIED TO PATIENTS WITH SUBSTANCE USE DISORDERS: COMPARISON WITH OUTPATIENT ENHANCED METHADONE SERVICE USING A CONTROLLED, PROSPECTIVE MATCHED PAIR-DESIGN.

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**Aims:** To evaluate the hypothesis that, for methadone maintained patients, day hospital (DH) treatment is more efficacious - in terms of health and psychosocial wellbeing - than standard outpatient (OP) setting.

DH provides more intensive care than outpatient settings and is less costly than full hospitalization. Studies on DH have shown mixed results; moderately burdened patients who chose their treatment deliberately may profit best from DH treatment. We prospectively compared OP with DH treatment of methadone maintained patients.

**Methods:** Out of 75 patients, only 16 + 16 individuals could be matched, mostly due to the higher proportion of outpatients on regular work. Urinalysis was done weekly for the first three months and then at follow-ups. Further outcome measures included: SUD-related problems and psychiatric symptoms (ASI), the BDI, the SCL 90-R, and the Social Support Inventory, administered at entry (t1), after the 14-week intervention period (t2) and at 6- (t3), and 12-month (t4) follow-up. DH treatment consisted of 5 to 25 hours (mainly group) therapy per week, whereas outpatients received between 1 and 3 hours of individual counselling. Data were analysed by t-test and General Linear Model for repeated measures.

**Results:** While both groups achieved higher employment rates, only DH patients showed significant improvements regarding social support and social problems. Symptom burden (SCL 90-R and BDI) decreased more clearly in DH patients though not statistically different. Substance use was lower in the DH-group, in particular during the first three months.

**Conclusions:** This study revealed some superiority of DH compared to OP treatment of methadone patients. Questions regarding differential indication and interventions remain to be answered. However, the DH treatment modality has proven efficacious in terms of medical, social, and vocational rehabilitation of methadone-maintained patient.

**Support:** The study was funded by the Swiss National Science Foundation.

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**LATE INJECTION DRUG USE INITIATORS: EPIDEMIOLOGICAL TRENDS AND RISK FACTORS.**

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**Aims:** Background: Much of drug prevention efforts have been aimed at preventing initiation of drug use among youth and young adults. Less attention has been paid to escalation from less dangerous to more dangerous drugs or to drug use with more dangerous administration routes (e.g. injection). Lastly, little effort has been devoted to preventing drug use escalation and uptake of drug injection among adults over the age of 30.

**Aim:** To assess trends in prevalence of and risk factors for late drug injection initiation among injection drug users (IDUs) in San Francisco.

**Methods:** Methods: The Urban Health Study was a serial cross-sectional study using targeted sampling methods to recruit IDUs in San Francisco from 1986 to 2005 (N=19,000). We consider anyone who initiates injection drug use after their 30th birthday as being a "late initiator," and assessed trends in the prevalence of late initiation as well as risk factors for late initiation.

**Results:** Results: The prevalence of late initiation among IDUs over the age of 30 was stable between 13% and 15% from 1989 to 2005. Factors associated (p<0.05) with late initiation included being female, African American, and lesbian/gay.

**Conclusions:** Conclusion: One in seven IDUs over 30 years of age initiated injection drug use after they turned 30 years old. Since 1989, there has been no change in percentage of IDUs who initiate injection drug use after age 30. Efforts to prevent late initiation of drug injection appear warranted. In addition, assessment of substance abuse treatment needs in this population is required. Social determinants associated with being a member of vulnerable social networks may be a central factor in promoting late initiation to injection. This suggests the value of further mixed methods exploration of this topic using cross-methodological social science theory.

**Support:** This research was supported by NIDA 1R01DA021627.

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**A NOVEL CUE REINSTATES EXTINGUISHED COCAINE-SEEKING BEHAVIOR.**

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**Aims:** The capability of cocaine-paired cues to generate craving in cocaine-dependent humans, even after extended periods of abstinence, is modeled in rats using cue reinstatement of extinguished cocaine-seeking behavior. The purpose of this study was to examine the specificity of cue reinstatement by comparing reinstatement of extinguished responding by cocaine-paired versus novel cues.

**Methods:** We trained two squads of rats to self-administer cocaine paired with either a light or a tone cue. The rats then underwent daily extinction training, during which lever presses produced no consequences and responses extinguished over time. Cocaine-seeking was then measured as an increase in lever presses performed by rats who received response-contingent cocaine-paired cues on their test day (i.e., Conditioned Cue Group), compared against the lever presses performed by rats who received response-contingent novel cues (i.e., Novel Cue Group). The light was used as the test cue for the Novel Cue rats previously trained with the tone, and the tone was used as the test cue for the Novel Cue rats previously trained with the light. All rats trained to self-administer cocaine were paired with control rats receiving yoked saline infusions.

**Results:** Unexpectedly, we found that rats in the Novel Cue Group reinstated cocaine-seeking behavior as well as rats in the Cues Group (2 x 2 ANOVA, baseline vs. test day as one factor, novel cues vs. conditioned cues as the other factor). The saline-yoked control rats did not exhibit significant lever pressing during the test session.

**Conclusions:** These results suggest that the reinstatement of cocaine-seeking behavior is achievable by exposure to novel as well as cocaine-paired cues.

**Support:** Supported by DA11064 and DA021485.

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**LONG-ACTING VS. ORAL NALTREXONE FOR PREVENTING HEROIN ADDICTION RELAPSE.**

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**Aims:** Naltrexone is the only medication approved in Russia for preventing relapse, however adherence to the oral formulation is a problem.

**Aim:** Compare long acting surgically implantable naltrexone(Prodetoxon) vs. oral naltrexone and placebo.

**Methods:** 190 consenting detoxified heroin addicts were randomized to 6 months of biweekly drug counseling under double-blind/double-dummy conditions to: Naltrexone 1000 mg implant every other month + Oral placebo daily (NI+OP; 66 SS); Placebo implant + Oral naltrexone 50 mg/day(PI+ON; 62 SS), and double placebo (PI+OP; 62 SS). Urine drug testing and psychiatric evaluations were done at each biweekly visit with more extensive evaluations at 3 and 6 months. Oral medication compliance was evaluated using a urine riboflavin marker.

**Results:** 218 patients were approached, 192 gave informed consent, and 190 were randomized. Treatment Effectiveness Score (TES; a sum of heroin positive and missed urines) revealed a clear advantage of the NI+OP group over the 2 others (p<0.01). At the end of six months, the TES in NI+OP patients was 63% compared to 87% in PI+ON and 86% in PI+OP. Survival analysis revealed greater retention in NI+OP compared to the two other groups (p<0.01). The number of non-surgical adverse events was limited with no difference between groups, however wound infections and local site reactions were higher in the NI+OP group (6% of all implants) compared to the other two groups (1%). This difference may have resulted from a few NI+OP patients trying to remove the implant. All infections were localized and resolved with antibiotic treatment.

**Conclusions:** The naltrexone implant was safe and more effective than oral naltrexone and placebo. Sustained release formulations are likely to improve the poor results typically obtained with oral formulations in treating heroin addiction.

**Support:** NIDA Grants:DA013043;DA-017317;DA-017009

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**ONE YEAR OF SUSTAINED-RELEASE NALTREXONE TREATMENT FOR OPIOID DEPENDENCE.**

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**Aims:** The aim of this study was 1. to evaluate the efficacy of implantable 6-month naltrexone pellets in an open RCT and 2. to investigate long-term effectiveness of the same implants in a second 6-month period that was not randomized.

**Methods:** 56 patients were included and randomized to receive or not receive a 6-month naltrexone implant in addition to their usual follow-up. After 6 months, participants could choose to receive or decline an implant for the 6-12 month period of the study. Drug use and other outcomes were assessed at 6- and 12-month follow-up using the Addiction Severity Index, Beck Depression Inventory, visual analog scales, and the Temporal Satisfaction with Life Scale. Hair samples were collected to verify self-reported opioid use.

**Results:** At 6 months, naltrexone patients had on average 45 days less heroin use and 60 days' less opioid use than controls in the 180-day period (both p<0.05). Blood tests showed naltrexone levels above 1ng/ml for the duration of six months. Hair samples confirmed patients' accounts in 37/43 cases. Two patients died, none of whom had received implants. Three implants were removed, two of which were on patients' requests. At crossover, 25/53 patients received an implant. 12-month results showed greater within-group variation in results and thus no significant differences between implant and no-implant groups.

**Conclusions:** Sustained-release naltrexone is confirmed in the randomized part of the trial as an effective treatment in reducing heroin use. Results of the second part of the study suggest that more than 6 months' treatment is necessary to maintain treatment gains for all but the most resourceful of patients.

**Support:** The Eastern Norway Regional Health Authority, The Norwegian Centre for Addiction Research at the University of Oslo, Norway.

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### GENDER DIFFERENCES IN SUICIDAL IDEATION AND OPIOID-USE DISORDER AMONG NON-MEDICAL OPIOID USERS WITH LIFETIME MAJOR DEPRESSION.

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**Aims:** Prior research has shown a high comorbidity between depression and non-medical opioid use disorder (dependence and/or abuse). This study examined the role of lifetime suicidal ideation in opioid use disorder among past year non-medical opioid users who have ever experienced major depressive episode, and if this relationship varies by gender.

**Methods:** Data from 1,509 adult respondents from the 2005 (n=37,227) and 2006 (n=36,965) National Survey on Drug Use and Health (NSDUH) who used non-medical opioid in the past year and had ever experienced major depressive episode. DSM-IV criteria were used to identify individuals who had past year non-medical opioid use disorder. Multivariate logistic regression taking into account the complex survey design was conducted to examine the relationship.

**Results:** Twenty-six percent of 5,775 past year non-medical opioid users reported lifetime major depressive episode (41% were males). Of these individuals, 195 (19%) female opioid users and 127 (23%) males opioid users met criteria for past year opioid use disorder. Female opioid users who have ever reported suicidal ideation were two times more likely to meet criteria for past year opioid use disorder [AOR (95%CI): 2.0 (1.2-3.2)]. This relationship remained after accounting for sociodemographic characteristics and number of other substance use disorders. In contrast, lifetime suicidal ideation was not associated with opioid use disorder among male non-medical opioid users in the multivariate model [AOR (95%CI): 0.8 (0.4-1.5)].

**Conclusions:** A gender-specific association between suicidal ideation and opioid use disorder exists among non-medical opioid users with lifetime major depression. Further examination of this relationship in a longitudinal setting may help sharpen identification efforts of those at risk for developing opioid use disorder. **Support:** NIMH T32MH14592 (Kuramoto), NIDA DA020667 (Martins), NIDA DA023434 (Martins) and NIA F31AG030908-02 (Ko)

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### PREWEANLING RATS EXHIBIT DEFICITS IN PREPULSE INHIBITION OF THE STARTLE REFLEX WHEN GESTATIONALLY EXPOSED TO NICOTINE.

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**Aims:** Maternal smoking during pregnancy has been correlated with deleterious outcomes for the offspring. The present study sought to determine the effects of prenatal nicotine (NIC) exposure on the pre-attentive process of prepulse inhibition (PPI). This procedure assesses an animal's ability to inhibit a startle response based on the perception of a stimulus that precedes the superthreshold startle stimulus.

**Methods:** Dams were administered 0.05 mg/kg of NIC (3x/day) through jugular catheters on gestational days 8-21. Pups underwent PPI trials on postnatal days (PND) 14 and 18 (N=36). Two prepulse modalities were used; auditory (85 dB) and tactile (16 psi airpuff) which preceded a 100 dB startle tone. Both modalities were assessed during the same session at 6 different interstimulus intervals (ISI); 0, 8, 40, 80, 120, and 4000 ms with 6 trials at each ISI using a Latin square design. The startle response (Vmax) was recorded by an accelerometer.

**Results:** Significant main effects of Gestational Treatment (Gest)  $F(1, 34) = 8.69$ ,  $P < .01$ , Age  $F(1, 34) = 9.37$ ,  $P < .01$ , Modality  $F(1, 34) = 22.48$ ,  $P < .001$ , and ISI  $F(3, 102) = 8.08$ ,  $P < .001$  were found. The main effect of Gest indicated that NIC animals did not inhibit as well as saline animals. A main effect of Modality revealed NIC animals were less able to inhibit compared to controls with auditory, but not tactile, prepulses. This was confirmed by a significant 3-way interaction of Modality x ISI x Gest  $F(3, 102) = 3.61$ ,  $P < .05$ . Lastly, inhibitory responses changed across Age. In general, animals showed greater inhibition at PND18; however, NIC animals showed little change across test ages with auditory prepulses.

**Conclusions:** Prenatal NIC impaired PPI with auditory, but not tactile prepulses. Some studies propose changes in nicotinic acetylcholine receptor densities as a possible mechanism for decreased auditory processing ability. The specificity of the disruption of PPI by NIC suggests that the alterations in neural circuitry underlying PPI must lie within central auditory processes.

**Support:** NIDA Grant DA 21287

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### PARTYING ON RX: CHANGES IN PRESCRIPTION DRUG USE AND MENTAL DISTRESS IN A NATURAL HISTORY STUDY OF CLUB DRUG USERS.

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**Aims:** To examine changes in prescription (Rx) drug use and mental distress (MD) over time among a sample of 601 club drug users and to investigate demographic differences. Data are drawn from an ongoing natural history study of club and Rx drug abusers. Hypotheses: 1) Rx drug abuse predicts MD at baseline; 2) changes in drug use predict changes in MD; and, 3) these patterns by race/ethnicity and gender.

**Methods:** MD was measured using a composite scale including somatic, depressive and anxiety symptoms. Growth curve models were estimated to assess changes in MD based upon time invariant (e.g., gender, age) and time variant (e.g., frequency of Rx opioid use) predictors. The analyses utilized the available sample at each time point (baseline N=601; 6-month N=481; 12-month N=365, 18-month N=255).

**Results:** Median age = 23; 22% Black, 21% White, 54% Hispanic; 59% male. Drug use and MD trended downward over time. Heavier Rx drug use predicted higher MD, but patterns differed by drug type and demographics. Heavier opioid use predicted increased MD for males but not females ( $p < .05$ ), while heavier use of benzodiazepines predicted increased MD for both ( $p < .05$ ). Older and Hispanic users reported higher levels of MD, controlling for other factors ( $p < .05$ ). Both opioid and benzodiazepine use raised the slope of the growth curves ( $p < .05$  at each time point), indicating that heavier users of either drug showed less improvement on the MD scale over time.

**Conclusions:** Overall patterns of decline in drug use over the follow-up periods are likely due to: 1) an intervention effect of the comprehensive assessments, and/or 2) an "aging-out" process from the club scene. Nevertheless, Rx drug abuse appears to present important mental health risks for recreational users. In addition to observed demographic differences in the MD consequences of abuse, the results point to potentially long term mental health problems from heavy Rx opioid and benzodiazepine abuse.

**Support:** This research was supported by Grant Number R21DA019840 from the National Institute on Drug Abuse.

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### NEURAL CORRELATES OF AGGRESSIVE RESPONDING IN ALCOHOL-DEPENDENT AND CONTROL SUBJECTS.

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**Aims:** Alcohol-related human aggression is a well-documented, complex and problematic phenomenon with profound public health consequences. Studying this relationship by merging methodologies in brain imaging and laboratory behavioral science will further scientific understanding of this complex phenomenon. Here we apply functional magnetic resonance imaging (fMRI) to examine neural correlates that mediate the relationship between human aggressive behavior and chronic alcohol abuse.

**Methods:** This ongoing experiment utilizes a laboratory model of human aggressive behavior (the Point Subtraction Aggression Paradigm, or PSAP) adapted for use during fMRI, to study differences in brain networks underlying aggressive behavior among alcohol dependent and matched healthy control participants. BOLD activation is measured during bouts of operationally-defined aggressive behavior (provoked by monetary subtractions) relative to responding on a different option that produces monetary earnings.

**Results:** To date, 6 subjects meeting DSM-IV criteria for lifetime alcohol dependence and 6 healthy controls have completed the protocol. All subjects were drug and alcohol free on testing days. Alcohol dependent subjects averaged 58.02 (SEM 5.55) aggressive responses per provocation vs. 28.33 (7.76) for controls. Whole brain random effects nonparametric analyses reveal significant group differences in limbic lobe/posterior cingulate (alcohol > control), insula, orbitofrontal cortex and prefrontal cortex (control < alcohol).

**Conclusions:** Individuals who abuse alcohol are at increased risk for aggressive behavior. Here we submit preliminary evidence, under controlled laboratory/imaging conditions, demonstrating that individuals who are recently alcohol-dependent show higher levels of aggressive responding and differences in BOLD activation in brain regions known to correspond to emotion, behavioral control, and anger.

**Support:** Supported by NIH R01 AA16965 and R01 DA03166

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**PATTERNS OF PRESCRIPTION DRUG MISUSE AMONG HIGH-RISK YOUTH.**

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**Aims:** Prescription drug misuse has become a primary public health concern in the U.S. due to increasing numbers of users and deleterious outcomes associated with abuse. Current rates of prescription drug use are highest among young people, yet descriptive data among high-risk youth are limited.

**Methods:** Data are based upon 27 (final n=150) prescription drug users aged 16 to 25 who were recruited in Los Angeles and New York during 2008. Sampling was stratified based upon recent histories of polydrug use, homelessness, or injection drug use (IDU). Semi-structured interview questions focused on misuse of prescription drugs and health risks.

**Results:** Across all three groups, misuse was frequently opportunistic and drugs were rarely paid for. Current misuse was often linked to friends or family members who possessed prescriptions. Many were raised by parents who misused prescription or hard drugs, and most were prescribed medications as children. Among IDUs, opioids were the primary prescription drug of choice, which were sometimes used as a substitute for heroin, and opioid overdoses were reported. Among homeless youth, marijuana was reportedly combined with prescription drugs - sometimes to medicate chronic pain. Among polydrug users, all had tried opioids though CNS depressants were more commonly preferred. Limited hard drug use was described and none reported an overdose.

**Conclusions:** Overall, patterns of misuse were often embedded in histories of family or prescribed use. Differences by subgroups were found: IDUs engaged in higher risk practices with more addictive prescription drugs; homeless youth reported chronic pain as a rationale for use; and polydrug users tended to use prescription drugs in a more occasional manner. Variations between groups suggest the need for targeted interventions to minimize negative health consequences associated with prescription drug misuse among high-risk youth.

**Support:** National Institute on Drug Abuse (R01 DA021299)

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**USING COACHES TO DEVELOP EBP SKILLS FOR PROVIDERS TREATING PATIENTS WITH CO-OCCURRING MENTAL HEALTH AND SUBSTANCE USE DISORDERS.**

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**Aims:** In November, 2007, UCLA's Integrated Substance Abuse Programs received a contract from Los Angeles County Department of Mental Health to provide COD training to staff working with Children ages 0-15 and their caregivers. In order to maximize skill development, a training strategy employing experiential classroom training combined with onsite consultation with a coach/mentor was employed. This presentation will focus on experience of providers receiving these coaching services.

**Methods:** Surveys were sent to 30 mental health program directors whose staff were receiving weekly coaching to assist in the development and reinforcement of COD knowledge and skills. Program directors were asked to distribute the surveys to all staff members who actively participated in coaching sessions.

**Results:** A total of 120 surveys were completed by counselors/social workers (74%), program managers (15%), parent advocates (5%) and others (6%). Participants were satisfied or very satisfied with the quality of the coaching (92%) and materials (86%). Respondents felt that the coaching improved rapport (84%) and helped them to monitor client progress (78%). Participants agreed/strongly agreed that the coaches provided consultation specific to their cases (90%) and assisted with effectiveness in Motivational Interviewing (78%), brief interventions (71%) and CBT strategies (73%). However, 41% indicated that coaching took time from other important activities. Additional quantitative and qualitative results will be provided.

**Conclusions:** Using coach/mentors to facilitate development of skills appears to be acceptable to providers to help them to develop concrete skills for working with COD patients.

**Support:** This project was generously supported by the Los Angeles County, Department of Mental Health, Contract #MH010054

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**PRESCRIPTION OPIATE USE AS A PROTECTIVE FACTOR FOR OTHER DRUG AND ALCOHOL USE IN HIV POSITIVE METHADONE PATIENTS.**

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**Aims:** Methadone patients admit to using prescription opiates (Rosenbloom et al, 2007). The present study explored the use of prescription opiate medication and its correlates in a sample of HIV positive methadone maintained individuals enrolled in a Directly Administered Antiretroviral Therapy (DAART) intervention.

**Methods:** Subjects in our sample (N=17) were administered baseline assessments including a timeline follow-back measure of 14-day drug use and medication adherence. To examine drug use of the subjects during the first three months of the DAART intervention, timeline follow back data from bi-weekly assessments were combined. Analysis of Variance Analyses (ANOVA) was performed to compare other drug use in those who were prescribed opiates to those who were not.

**Results:** Our sample consisted of 10 men, 5 women, and 2 transgender individuals; 41.2% identify as Hispanic, 23.5% as African American, 29.4% as white and one as other. More than 75 percent (n=13, 76.5%) of the sample was prescribed opiate pain medications. At baseline, participants who received prescription pain medications had fewer days of alcohol use (M=2.08, SD=4.55) than those who did not [(M=8.00, SD=5.72), (F(1,16) = 4.64, p<.05)], while no significant differences in marijuana use, heroin use, or cocaine use were found. After 3-months of participation in the DAART intervention, days using alcohol was no longer significantly different in those who were prescribed opiate medications from those who were not, yet number of days using marijuana was significantly higher in those who were not prescribed opiate medication [(M=39.75, SD= 36.44 vs. M=6.58, SD=10.16), (F(1,15)=14.40, p<.01)].

**Conclusions:** There is a high rate (over 75%) of prescription opiate use in the current sample. More research is needed to determine whether prescribed opiates can reduce other drug and alcohol use, with lower alcohol and marijuana use among those prescribed opiate medications in addition to methadone.

**Support:** R21DA020369, 5T32MH018261

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**HIV PREVENTION USING A DYADIC AND NETWORK INTERVENTION: THE STEP STUDY.**

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**Aims:** Injection drug users continue to have high rates of HIV in the U.S. Moreover, many injection drug users acquire and transmit HIV sexually. The present study was a network oriented intervention targeting injection drug users and their drug and sexual risk partners.

**Methods:** Participants were recruited through ethnography and outreach in inner-city Baltimore Maryland. The 6 session RCT included an equal attention control group. The intervention focused on HIV, HCV, and overdose prevention and included a dyadic session for injection drug users and their network members. Index participants in the experimental groups were taught to promote risk reduction among their network members. Index eligibility included current injection drug use and the ability to recruit at least one risk (drug or sex) network member. Participants were assessed at 6, 12, and 18-months. Retention rates were over 80% at 18 months.

**Results:** At baseline 1,024 participants were interviewed; 60% male, and 34% had been homeless, 27% in prison, and 82% injected drugs in the prior six months. An-intent-to-treat analysis at the 12-month follow-up revealed less frequent sharing of cookers and cottons among the index intervention participants (who received the six experimental sessions) as compared to those in the control group. Those in the intervention condition also reported more frequent use of safe drug splitting equipment. A similar pattern was found among the network members of the indexes in the experimental condition as compared to the network members of the indexes in the control condition.

Moreover, at the 12-month assessment, there was a tendency for the index participants in the experimental group compared with those in the control group to report that they had not used opiates or cocaine in the prior six months (33% vs. 18%).

**Conclusions:** The results of this study suggest that active drug users can be taught to be positive change agents and promote safer injection behaviors within their risk networks and out in the community. The results also suggest that social networks may be effective vehicles for promoting behavior change.

**Support:** NIDA- DA016555

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**LONGITUDINAL PATTERNS AND CORRELATES OF SMOKING IN FORMERLY POLYSUBSTANCE DEPENDENT INDIVIDUALS.**

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**Aims:** Smoking often co-occurs with substance use disorders. We lack information on the prevalence, correlates and longitudinal patterns of smoking among persons in recovery. Though several states have enforced smoking bans in substance abuse treatment programs, they reach but a fraction of the recovery community that may remain at elevated risk for the many nefarious consequences of smoking. We examine (1) Longitudinal trends in smoking; (2) Association of tobacco use with duration of abstinence from or use of other substances; and (3) Correlates of these patterns, in a prospective sample of formerly polysubstance dependent persons.

**Methods:** Community-based polysubstance dependent persons who were drug abstinent for 15.6 months (Mdn) at intake (BL) were re-interviewed yearly for 3 years about drug, alcohol and tobacco use (83% retention at F3; full dataset N=285, 44% women, 63.6% African American).

**Results:** At BL, 69.5% of subjects reported current use of tobacco products, mostly cigarette smoking. Smoking was significantly ( $p < .05$ ) more prevalent among persons in early recovery and in younger participants, and at the trend level ( $p < .1$ ) in non-whites and females. Smoking had become more important since quitting drug use for 31.8% of subjects. Smoking prevalence did not change significantly during the 3-year study but intra-individual changes were noted in 22.5% of subjects: 8.8% started smoking, 8.8% stopped, 4.9% stopped and started again. Being continuously drug abstinent (biologically corroborated) over the entire study period was significantly associated with abstaining from smoking during the same period.

**Conclusions:** Smoking prevalence in this sample of former polysubstance users was more than twice the national rate and there were few (failed or successful) attempts to quit over the 3-year study. Smoking may start or increase after entering recovery. Smoking prevention and cessation efforts are critically needed in this population and should be integrated in specialty care and in recovery support services; physicians must also address smoking cessation with patients who have a history of substance use disorders.

**Support:** R01 DA014409

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**GROUP REALITY THERAPY: IS IT AN EFFECTIVE TOOL IN WORKING WITH OPIOID-DEPENDENT YOUNG ADULTS IN METHADONE MAINTENANCE TREATMENT?**

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**Aims:** To present the theoretical basis for utilizing Reality Therapy in group work with opioid dependent young adults, to describe the intervention and to assess its effectiveness.

**Methods:** Group work based on Reality Therapy is utilized in the Haifa Drug Abuse Treatment Center in Israel as a major tool for treating young adults (ages 21-27). An ongoing Reality Therapy group for young adults, led by two Master level social workers, is followed over 6 months of group work. The process and intervention are recorded.

**Conclusions:** This study will describe and examine the effectiveness of group Reality Therapy with opioid dependent young adults receiving Methadone maintenance treatment. Personal characteristics of group participants will be detailed. The design and the actual group process that took place will be described. Finally, the effectiveness of the intervention will be assessed on the basis of pre-post measures regarding stability on Methadone, criminal activity, social interaction and employment. Implications for policy and practice will be discussed.

**Support:** This work is supported by internal funds of the Haifa Drug Abuse Treatment Center.

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**PSYCHIATRIC COMORBIDITY, SEVERITY OF ADDICTION AND QUALITY OF LIFE IN OPIATE DEPENDENT TREATED PATIENTS: A ONE-YEAR PROSPECTIVE STUDY.**

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**Aims:** To study, in naturalistic conditions, initial characteristics and one year outcome of clinical status and quality of life, among opiate-dependent patients in methadone and buprenorphine treatment.

**Methods:** Consecutive opiate-dependent patients admitted to an outpatient addiction clinic in Bordeaux (France) and still in treatment at one year were included. Subjects were assessed at intake and one year later with the Addiction Severity Index (ASI), the Nottingham Health Profile (NHP). Beck anxiety and depression inventories (BAI, BDI), Zuckerman Sensation Seeking Scale (SSS), and urine drug screening was performed. We studied associations between psychiatric comorbidities, sensation seeking traits, clinical factors and quality of life, at intake and over the one year period. Parametric and non parametric univariate and multivariate analysis was used.

**Results:** 134 subjects were included (mean age 31.8 years (SD= 5.8), 75 % males). At intake, according to the ASI, the prevalence of psychiatric disorders was high. Psychiatric comorbidity was associated with severity of addiction and quality of life impairment. At 1-year follow-up, subjects showed improvement in substance use, legal issues, familial relations, social relations, psychological conditions and overall quality of life. Sensation seeking traits were not associated with clinical outcomes. Subjects' initial psychological status did not affect clinical outcome with respect to the above characteristics at 1-year. At 1 year, in multivariate regression, improvement in quality of life was related to fewer symptoms of depression and better medical status, but was not related to substance use.

**Conclusions:** Results suggest that psychological status at intake does not impair outcome in treatment.

**Support:** PHRC 2000, 2006. MILDT-INSERM 2004.

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**PARTIAL ABLATION OF MU-OPIOID RECEPTOR RICH STRIOSOMES RESULTS IN BEHAVIORAL DEFICITS ON A MOTOR SKILL LEARNING TASK.**

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**Aims:** In mice, striosomes are rich in mu opioid receptors (MOR) and form a 3-dimensional labyrinth of cells that are embedded in an extrasomal matrix and extend from the mid to anterior striatum. While the functional role of these MOR-rich striosomes is not well understood, some evidence suggests that administration of apomorphine, cocaine, amphetamine or electrical self-stimulation results in an activation of striosomal neurons that corresponds to aberrant motor output.

**Methods:** To investigate the relationship between the striosomes and motor behavior we used the MOR-specific toxin dermorphin-saporin (DS) to selectively ablate striosomal cells. FVB mice were bilaterally infused with DS in the mid striatum alone or in the mid and anterior striatum simultaneously, and were tested on a battery of behavioral tests before and after the infusion. 3D reconstructions and unbiased stereology was used to count the cells and measure the volume of the striosomes and the surrounding matrix.

**Results:** Mice that received DS injections showed the smallest volume and fewest cells in the striosome compartment compared to mice that received control injections of saline or saporin. Striosome volume and cell loss was greatest in the dorsolateral striatum. The extrasomal matrix was not significantly affected. Mice that received DS injections also showed deficits on an accelerating rotarod task and the deficit was worse in mice that received mid and anterior injections than those that received mid striatal injections alone. However, DS injected mice did not differ from control mice on other motor tasks.

**Conclusions:** We conclude that striosomes in the dorsolateral striatum are necessary for optimal performance on the rotarod task and that striosomes mediate a type of motor output in rodents that may contribute to our understanding of motor learning and reward circuits.

**Support:** R01 21356;F31 NS055592-02



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**IMPULSIVITY, COMPLETION STATUS, AND ETHNICITY IN A CLINICAL TRIAL FOR COCAINE DEPENDENCE.**

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**Aims:** To explore associations between impulsivity, demographic factors, and completion status among subjects seeking treatment in a cocaine dependence clinical trial.

**Methods:** The Barratt Impulsivity Scale (BIS-11) and the Impulsive scale from the Eysenck Impulsiveness, Venturesomeness, and Empathy Questionnaire (IVE-7) were collected during the screening phase of a double blinded trial of Modafinil for cocaine dependence. Standard impulsivity scores (expressed in percentiles) among different participant subgroups were compared with independent t-tests.

**Results:** Of the 102 participants screened, 59 were African American and 43 were Caucasian; 21 were ineligible to enter study, 23 failed to return in screening, 58 entered treatment, with 31 of those completing 8 weeks of treatment. African Americans had lower impulsivity than Caucasians on both instruments. African Americans had a mean percentile of 54 on the BIS-11, Caucasians had a mean percentile of 58 (p-value = .02). Additionally, completers had significantly lower IVE-7 Impulsivity scores (mean percentile of 42) than non-completers (mean percentile of 52) (p-value = .03). If we restrict our analysis to only the 58 subjects who entered treatment the same trends hold. Namely, mean percentile on the BIS for African Americans subjects in treatment was 53%, compared to 60% for white subjects in treatment (p-value = .003). Also, completers had lower IVE-7 Impulsivity scores (mean percentile 42%) compared to non-completers who entered treatment (mean percentile 56%) (p-value = .02).

**Conclusions:** African Americans seeking treatment for cocaine dependence were less impulsive than Caucasians, as measured by the BIS-11 and IVE-7. Additionally, participants who completed all 8 weeks of treatment were less impulsive than those who failed screening or dropped out of the study.

**Support:** Supported by grant # R01 DA019903 and grant # R01 DA016368 from the National Institute on Drug Abuse.

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**THE ACUTE EFFECTS OF COMBINED BENZYLPIPERAZINE AND TRIFLUOROMETHYLPHENYLPIPERAZINE ON HUMAN P300 EVENT-RELATED POTENTIALS.**

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**Aims:** Products containing benzylpiperazine (BZP) and trifluoromethylphenylpiperazine (TFMPP) have been marketed as a safe and legal alternative to methylenedioxymethamphetamine (MDMA/Ecstasy) and other amphetamines. It has been suggested that the combination of BZP and TFMPP mimics the neurochemical effects of low dose MDMA in rodents. Although BZP and TFMPP are frequently taken for recreational purposes there is little information available about their effects on human cognition. A double-blind, placebo-controlled study using electroencephalograph (EEG) was carried out to investigate the effects of BZP and TFMPP on attentional and memory processes using the P300 component.

**Methods:** Healthy, right-handed males (age:22±3 years) were given a single oral dose of placebo (n=18) or the combination of BZP and TFMPP (100mg, 30mg respectively, n=18) and tested both pre- and 2 hr post-drug administration. High-density EEG recordings (128 leads) were used to record event-related potentials (ERPs).

The P300 component was defined as the biggest positive peak in the range between 250-350 ms after the stimulus. The amplitude and latency of P300 were analysed using two-way repeated measures ANOVA.

**Results:** Surprisingly BZP and TFMPP caused no significant change in the P300 latency and the amplitude despite causing a significant elevation in mood, heart rate and blood pressure.

**Conclusions:** Previously studies conducted in our laboratory have found that BZP and TFMPP, when administered separately, reduce the P300 amplitude in humans. TFMPP is an agonist at 5-HT<sub>2C</sub> receptors which diminish mesolimbic dopaminergic neuronal firing. Consequently the dopaminergic effects of BZP on human cognition are likely to be antagonised by co-administration of TFMPP. The lack of significant effects may be due to neuropharmacological antagonism between the two compounds or an inability of ERP's to reliably characterise the effects of recreational drugs.

**Support:** Trecia Wouldes

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**REDUCED CARBON MONOXIDE IN TREATMENT-SEEKING CIGARETTE SMOKERS UNDERGOING CONTINGENCY MANAGEMENT: PRELIMINARY ANALYSIS.**

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**Aims:** Smoking-related illnesses are responsible for up to 1 in 6 deaths in the United States each year. Many smokers report a desire to quit smoking, but most who try are not successful. Although there are several effective behavioral and pharmacological smoking cessation interventions, no one treatment is effective for all smokers. In this report, we describe preliminary analysis of a prize-based incentive program for smoking cessation. We hypothesized that carbon monoxide (CO) levels during the CM treatment phase would be significantly reduced compared with CO levels at intake and the final CO assessment of the baseline phase (i.e., immediately preceding implementation of CM).

**Methods:** Smokers participated in an intake assessment, followed by a one-week baseline period and a four-week prize contingency management program in which they received escalating prize draws for providing twice-daily CO samples of < 6ppm. CO data are presented for 16 (13 women and 3 men; mean age 45.4 [SD=10.9]; mean Fagerstrom Test of Nicotine Dependence score 6.7 [SD=1.2]) nicotine dependent cigarette smokers who have completed CM treatment to date.

**Results:** Mean CO reading was 16.8ppm (SD=6.1) at intake and 7.6ppm (SD=3.4) at the final baseline session (CO average was 10.9 [SD=5.5] over the entire baseline week). Mean CO during the CM treatment phase was 4.0ppm (SD=3.9). Mixed-effects model analysis of intake and CM phase CO values showed significant time effects (F(40) = 9.90, p < .001). In pairwise comparisons, CO values at intake were significantly higher than each of the 40 data collection points during the CM phase (all p's < .001). Mixed-effects model analysis of the final baseline session and CM phase CO values also showed significant time effects (F(40) = 2.92, p < .001). CO values at the final baseline session were significantly higher than 34 out of the 40 data collection points during the CM phase (all p's < .05).

**Conclusions:** These findings suggest that prize-based CM results in reduced CO levels and that CM may be an effective treatment for smoking cessation.

**Support:** Supported by R21 DA021839-01A1

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**REWARD-SEEKING TASK PERFORMANCE: A VALIDATION STUDY.**

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**Aims:** Risk-taking behavior is associated with the initiation and development of regular drug use among adolescents and young adults. Both sensitivity to reward and inhibition are linked to risk-taking behavior, but only behavioral inhibition has been examined systematically in previous research. The purpose of this ongoing study is to examine individual differences in performance on tasks purportedly measuring reward-seeking behavior. Performance on three tasks is examined at different levels of monetary incentive in order to determine whether dimensions of behavior that are sensitive to incentive are (1) consistent among tasks, and (2) associated with personality dimensions of reward seeking.

**Methods:** Healthy young adult volunteers (N=40, anticipated completion of data collection: 03/2009) scoring in the top and bottom quartiles of gender-adjusted population norms on the reward-seeking items in the impulsive-sensation seeking subscale of the Zuckerman-Kuhlman Personality Questionnaire complete a 1-hour training session and a 4-hour experimental session consisting of performance on a Progressive Ratio task (PR), a Monetary Incentive Delay task (MID) and a Balloon Analog Risk Task (BART), each at three levels of monetary incentive.

**Results:** Initial results (n=4) indicate that task performance varies as a function of monetary incentive. Break points on the PR task, for example, increase as a function of incentive (\$0.01: 5.0 ± 1.2; \$0.10: 7.2 ± 0.5; \$1.00: 6.8 ± 0.9), while inflations per balloon on the BART decrease as a function of level of incentive (\$0.003: 62 ± 11; \$0.01: 53 ± 9; \$0.03: 39 ± 5).

**Conclusions:** Performance on the BART and MID and PR tasks varies with level of incentive. Regression and correlation analyses of performance across incentive conditions will be conducted to examine the sensitivity and consistency of task measures of reward sensitivity, and mixed-model repeated-measure ANOVAs will be conducted to determine whether task performance is associated with individual differences in the personality dimension of reward seeking.

**Support:** Supported by DA-05312 and RR-15592.

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**STRIATAL DOPAMINE D2/D3 RECEPTORS, IMPULSIVITY, AND METHAMPHETAMINE DEPENDENCE.**

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**Aims:** Individuals who abuse stimulants are thought to be more impulsive than healthy comparison subjects, and cognitive test data indicate they also have deficits in inhibitory control. Animal studies suggest that deficiencies in striatal dopamine (DA) D2/D3 receptors are associated with impulsive (i.e., premature) responding and 'addiction-like behaviors', but the links between DA D2/D3 receptors, impulsivity and stimulant dependence in human subjects are not clear. Therefore, we compared methamphetamine-dependent (MA Group) and healthy comparison (HC Group) subjects on self-reports of impulsivity, motor response inhibition and striatal DA D2/D3 receptor availability; and tested relationships between these variables.

**Methods:** Fifty-three human subjects (33 men, mean age = 33, S.D. = 9) who met criteria for MA dependence and 67 healthy comparison subjects (37 men, mean age = 32, S.D. = 8) participated. The Barratt Impulsivity Scale was used as a measure of impulsivity and the Stop Signal Task was used to measure motor response inhibition. Striatal DA D2/D3 receptor availability was measured using PET and [<sup>18</sup>F]-fallypride in 15 MA subjects and 27 HC subjects.

**Results:** MA subjects had significantly lower DA D2/D3 receptor availability in striatal regions ( $F(3,38) = 5.33, p = 0.004$ ), higher self-reported impulsivity ( $F(3,116) = 12.223, p < 0.001$ ) and deficits in motor response inhibition ( $F(1,78) = 7.428, p = .008$ ) compared to HC subjects. Striatal DA D2/D3 receptor availability was inversely related to both measures of impulsivity.

**Conclusions:** The findings provide direct evidence that deficits in striatal DA D2/D3 receptors contribute to impulsivity and thereby, perhaps to stimulant dependence.

**Support:** DA15179, DA022539, DA020726, and RR00865

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**PSYCHOLOGICAL SYMPTOM SEVERITY IN A RESIDENTIAL SAMPLE OF WOMEN WITH SUBSTANCE USE DISORDERS.**

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**Aims:** Many drug treatment programs currently do not routinely assess for psychological distress in women with substance use disorders (SUDs). When such distress goes untreated, it can contribute to relapse and premature treatment drop-out. The present study compared psychological symptom severity in a residential treatment sample of SUD women to 3 normative samples.

**Methods:** Participants were 141 women who consented to a larger RCT. The Brief Symptom Inventory (BSI) was administered during baseline assessment. Most women were in their late 30's ( $M = 36.4$ ) and African American (63.6%). The BSI is a standardized 53-item measure of psychological functioning. The 9 BSI subscale scores obtained by the residential SUD women were compared to 3 normative groups: non-substance abusers; psychiatric inpatients; and outpatients with SUDs.

**Results:** Residential SUD women had higher scores on all 9 BSI subscales (all  $p < .01$ ). In contrast, residential SUD women had significantly lower scores on 5 BSI subscales when compared to psychiatric inpatients: Interpersonal Sensitivity, Depression, Anxiety, Hostility and Phobic Anxiety (all  $p < .05$ ). Finally, comparisons between residential and outpatient SUD patients found higher scores for the residential sample on 7 of the 9 BSI subscales (Obsessive-Compulsiveness, Interpersonal Sensitivity, Depression, Anxiety, Phobic Anxiety, Paranoid Ideation and Psychoticism) (all  $p < .05$ ).

**Conclusions:** Study findings further support BSI validity, with residential SUD women obtaining higher subscale scores than persons in the general population and outpatient clients with SUDs. The residential SUD women had lower scores, however, than a psychiatric inpatient sample. More importantly, the data affirm that SUD women in residential treatment present with significant levels of psychological distress and that interventions to reduce and treat such symptoms are sorely needed to reduce relapse and improve treatment effectiveness.

**Support:** Research supported by grants from the VCU Institute for Women's Health and NIDA R36 DA024021.

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**EXTENDED-RELEASE NALTREXONE FOR TREATMENT OF ALCOHOL DEPENDENCE IN PRIMARY CARE.**

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**Aims:** The feasibility of extended-release naltrexone injectable suspension (XR-NTX) for treatment of alcohol dependence in primary care is uncertain. We investigated 3-month treatment retention, patient satisfaction, and alcohol use among alcohol-dependent patients treated with XR-NTX in two urban public hospital medical clinics.

**Methods:** Eligible patients were alcohol-dependent adults seeking XR-NTX treatment and able to attend 3 monthly medical management (MM) sessions and one 4-month follow-up visit. MM emphasize eliminating drinking, accessing Alcoholics Anonymous (AA) and outside counseling, and treatment adherence. XR-NTX doses were monthly (380mg IM). Drinking quantity/frequency, side effects, and AA and counseling participation were tracked. A 7pt. scale of hedonic tone (perceived pleasure/taste) assessed enjoyment of alcohol, diet, and other activities at baseline then monthly. Visits and medication were free; patients received incentive (\$20) at Month 4.

**Results:** 72 patients were enrolled over 13 months from hospital inpatient (3), primary care (5), and alcohol outpatient programs (16), ads (39), and word-of-mouth (9). Patients were mean age 46 yrs.; 33% female; 18% black, 21% Hispanic; 31% uninsured. Monthly retention: 89% of eligible patients received 1st injection; 69%; 2nd injection; 56% completed 3 injections. Participants consistently reported reduced cravings and high satisfaction in-treatment. Percent of previous 30 days abstinent increased from 47% at baseline to 85% in-treatment. At Month 4, 60% of patients chose to remain on monthly naltrexone injections after study completion in a related 12-month extension study. Preliminary analysis of within-subject changes in hedonic tone indicated XR-NTX selectively diminished perceived enjoyment of alcohol while not altering that of food, exercise, or sex.

**Conclusions:** Extended-release naltrexone within a primary care monthly medical management alcohol treatment model appears feasible and acceptable.

**Support:** Financial support and study drug product for this study were provided by Alkermes, Inc./Cephalon, Inc. as part of an Investigator Sponsored Study program

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**NICOTINE CONDITIONED PLACE PREFERENCE IN ADOLESCENCE DIFFERS AS A FUNCTION OF SEX.**

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**Aims:** Although women now constitute half of all smokers and many studies suggest that adult males and females may differ in factors that maintain tobacco smoking, little is known about nicotine reward in adolescence. Laboratory studies show that adolescent male rats self-administer more nicotine than adults, and that adult females may be more sensitive to nicotine's reinforcing effects, however, there is little information available about sex differences in nicotine reward during adolescence. In the present study, sensitivity to the conditioned reward of nicotine was evaluated in male and female adolescent rats. The main hypothesis of this proposal was that females and males would respond differently to nicotine during adolescence.

**Methods:** Adolescent (PND 34) male and female rats were tested using a conditioned place preference (CPP) procedure. On the first day, a pretest was conducted to determine initial preference to both compartments of the chamber. The day following the initial preference test, conditioning began. During conditioning, rats received a saline injection and were placed into one compartment for 30 min in the morning. In the afternoon rats were treated with various doses of nicotine (0.2, 0.4, 0.6 and 0.8 mg/kg) and placed into the opposite side for 30 min. The day after the last conditioning session, a posttest was conducted and the time spent on each side was recorded for 30 min.

**Results:** Female rats were more sensitive than males to the conditioned rewarding effects of nicotine. In fact, adolescent male rats did not develop a significant CPP to nicotine at any dose under multiple training and testing conditions.

**Conclusions:** During adolescence, sex determines the vulnerability to nicotine reward. These findings suggest that it will be necessary to take this into account in the development of sex- and age-specific strategies for improving smoking cessation treatments.

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**EFFECT OF MODAFINIL ON STRESS-INDUCED COCAINE SEEKING AND COCAINE CROSS-SENSITIZATION IN LABORATORY RATS.**

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**Aims:** Modafinil is a stimulant used to treat narcolepsy and other disorders involving excessive sleepiness. Because of its long-acting agonistic action on central monoamine systems, orexin and glutamate, modafinil is also being investigated as a potential "substitution" treatment for cocaine dependence, withdrawal and relapse.

**Methods:** We employed male Sprague-Dawley rats to explore whether chronic administration of modafinil (0, 25, or 50 mg/kg, IP, twice daily) could alter spontaneous cocaine seeking observed during extinction, and reinstatement of cocaine seeking precipitated by stress. Thus, rats were first trained to self-administer cocaine intravenously (0.25 mg/kg/infusion, 3h/day x 10 days), and then treated with modafinil prior to 7 extinction sessions whereby saline was substituted for cocaine, and prior to a test of reinstatement of lever-pressing by exposure to 15 min intermittent foot-shock stress (0.8 mA, 0.5 s ON, a mean OFF period of 40 s). Two additional studies assessed the effect of cocaine sensitization (20 mg/kg x 5 days) on the stimulatory and rewarding effects of modafinil (50 and 100 mg/kg).

**Results:** In the reinstatement study, it was found that modafinil had no effect on spontaneous and precipitated cocaine seeking, even though it produced significant stimulation. In the locomotion cross-sensitization experiment, it was found that the stimulatory properties of modafinil were significantly increased by chronic cocaine exposure, but cocaine sensitization did not enhance the rewarding properties of modafinil.

**Conclusions:** These results in laboratory rats do not support the effectiveness of modafinil in preventing relapse to cocaine seeking caused by stress, and further suggest that modafinil may have enhanced stimulatory properties in cocaine addicts. However, since its motivational properties were not altered by cocaine exposure, these data in rats also suggest that this drug may be a safe pharmacological approach to the treatment of cocaine withdrawal.

**Support:** Canadian Institutes of Health Research (CIHR)

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**EFFORT TO OBTAIN COCAINE MODULATES THE EFFECTS OF A DIFFERENTIAL-REINFORCEMENT-OF-ALTERNATIVE-BEHAVIOR SCHEDULE OF ALTERNATIVE NONDRUG REINFORCEMENT ON COCAINE SELF-ADMINISTRATION IN RATS.**

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**Aims:** We have been employing a differential-reinforcement-of-alternative-behavior (DRA) schedule of alternative nondrug reinforcement as potential model of contingency management interventions for drug abuse. We previously demonstrated that such a schedule decreased nicotine and cocaine self-administration in rats, but the effect on cocaine self-administration (CSA) was modest and required significantly higher rates of alternative reinforcement than that necessary to suppress nicotine self-administration. The current study examined the efficacy the DRA schedule under higher response requirements for CSA.

**Methods:** Rats were trained to self-administer cocaine (0.3 mg/kg/inf) under a fixed-ratio (FR) 3 or 9 schedule of drug delivery. After stable CSA was obtained, an interlocking DRA schedule of sucrose delivery was implemented. Under this schedule, cocaine continued to be available under the FR schedule while a sucrose pellet was made available contingent upon every pause in self-administration responding (DRA interval) of 10, 20, or 40 sec. Pellet availability was signaled by a tone, at which point a pellet was delivered if the sucrose lever was pressed.

**Results:** Under the FR 3 schedule of CSA, the DRA schedule produced a small but significant decrease in CSA only at the shortest DRA interval. Under the FR 9 schedule of CSA, significant suppression of CSA was observed at all DRA intervals. Within-session analysis indicated that, in several rats, sucrose-maintained responding dominated early in the session, followed by a distinct shift to CSA for the remainder of the session.

**Conclusions:** The present findings are consistent with prior studies showing that the efficacy of alternative nondrug reinforcement in reducing drug self-administration is increased when response requirements for drug are increased. DRA schedules of alternative reinforcement may be useful for examining factors that may mediate the efficacy of CM interventions.

**Support:** NIDA Grant R01-DA020136

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**THIRTY DAY OUTCOMES: A RANDOMIZED TRIAL OF WOMEN'S RELATIONSHIPS AND HIV.**

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**Aims:** This study presents outcomes for a trial to change relationship characteristics, HIV risk behaviors and HIV knowledge among women prisoners re-entering the community. The HIV infection rate is higher among women prisoners than the general population (Maruschak, 2004). Relationships are important because women adapt their sexual behaviors to their partners (Covington, 1998). But little is known about the association of partner relationships and HIV.

**Methods:** Data were collected at 30 day community follow-up during the Reducing Risk Relationships (RRR) for HIV trial from women inmates as part of the NIDA CJ-DATS cooperative. Knowledge of HIV Risk behaviors, Condom Self-Efficacy (Braford & Beck, 1991) and relationships were compared for the intervention vs. the control group using t-tests and effect size.

**Results:** 447 women completed the baseline interview; 381 were eligible for follow up at 30 days post-release, of which 352 (92%) were interviewed. About half (51%) were randomized to the RRR intervention group. The median age was 35.9 years (IQR: 28.6, 43.3), and the majority were white (71%). Before prison, women reported daily use of crack (37%), alcohol (27%), and marijuana (24%). At 30-day follow-up, compared to the control group, women in the RRR experimental group reported more knowledge: HIV can be transmitted by injection paraphernalia (effect size [ES]=0.41, p<0.001); use of crack may increase risk for HIV (ES=0.26, p=0.018); male and female condoms should not be used together (ES=0.77, p<0.001); and drug use may lead to unhealthy choices about protection (ES=0.41, p<0.001). Women in the RRR group also reported significantly greater Condom Self-Efficacy than those in the control group (ES=0.24, p=0.029).

**Conclusions:** The RRR intervention at 30 day follow-up increased HIV knowledge, condom self-efficacy, and relationship characteristics for women prisoners after community re-entry which underscores the importance of providing effective interventions that address women's relationships.

**Support:** NIDA 5U01DA016205

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**THE CONTRIBUTION OF THE QUALITY OF STAFF-PATIENTS' RELATIONSHIPS TO PATIENTS' SATISFACTION WITH METHADONE SERVICE.**

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**Aims:** This study explores the associations between quality of patient-staff relationships, as perceived by the patients, and their satisfaction with service.

**Major Hypotheses**

1. The better perceived the quality of patient-significant staff member relationship, the higher the patient's general satisfaction with the service.
2. Higher dosages are associated with greater patient satisfaction. Number of visits per week is associated with lower satisfaction

**Methods:** 197 of 284 (69.4%) patients in one large methadone clinic in Israel were questioned about their satisfaction with service and their relationship with one significant staff member, if any. We used a structured interview with scales ranging from 1 point (low satisfaction/evaluation) to 5 points (high satisfaction/evaluation).

**Results:** Satisfaction- Patients' general satisfaction with service was high, with lower rates among patients from the Former Soviet Union and Arabs than among Jewish Israel-born patients.

All but three patients reported having a significant relationship with a staff member.

Methadone dosage was not associated with patients' satisfaction; and the greater the number clinic visits, the lower their satisfaction.

Hierarchical linear regression—controlling for background variables, duration treatment, illicit drug use, methadone dose, number of weekly clinic visits, and number of activities participated—revealed that the quality of relationships between patient and significant staff member was significantly associated with patients' general satisfaction with the service, contributing additional 7% for the explained variance (total explained variance, R<sup>2</sup>, was .33).

**Conclusions:** Examining patients' satisfaction in drug treatment services should shift from patient characteristics to the quality of interactions with staff

**Support:** Association for Public Health Services

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**ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND NICOTINE WITHDRAWAL SYMPTOMS AMONG TREATMENT-SEEKING ADOLESCENT SMOKERS.**

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**Aims:** Individuals with ADHD are more likely than their non-ADHD counterparts to initiate smoking and develop nicotine dependence. Recent research indicates that adults with ADHD experience more severe nicotine withdrawal symptoms than those without ADHD. However, little is known about nicotine withdrawal in adolescent smokers with comorbid ADHD.

**Methods:** Among a sample of 134 nicotine-dependent adolescents entering a smoking cessation research study, 47 met DSM-IV criteria for ADHD. All participants completed the Minnesota Nicotine Withdrawal Scale (MNWS) during their initial assessment. Responses on individual items and MNWS total score were compared between ADHD and non-ADHD participants.

**Results:** Adolescent smokers with ADHD scored significantly higher on the MNWS total score than those without ADHD ( $p < 0.001$ ). Among the individual items within the MNWS, ADHD participants were significantly more likely to endorse symptoms of depressed mood ( $p = 0.012$ ), insomnia ( $p = 0.047$ ), difficulty concentrating ( $p = 0.002$ ), restlessness/impatience ( $p = 0.002$ ), and increased appetite ( $p = 0.014$ ). They were additionally more likely to report high levels (3+ response) of irritability/frustration/anger ( $p = 0.016$ ) and anxiety/nervousness ( $p = 0.011$ ).

**Conclusions:** Treatment-seeking adolescent smokers with ADHD are more likely to endorse nicotine withdrawal symptoms than those without ADHD. However, it is unclear if the symptoms reported in this sample represent a valid "withdrawal syndrome," particularly because these smokers had not yet formally attempted to quit. The data may instead reflect common features between ADHD and nicotine withdrawal. Smoking research, particularly among adolescents in whom ADHD is so common, should carefully consider the complex issue of comorbid ADHD and nicotine dependence.

**Support:** Supported by NIDA (R01DA17460, R25DA020537, K12DA000357, K23DA020482) and USPHS (M01RR01070).

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**DIFFERENTIAL MODIFICATION OF THE ANTINOCICEPTIVE AND DISCRIMINATIVE STIMULUS EFFECTS OF MORPHINE BY 5-HT<sub>1A</sub> AND 5-HT<sub>2A</sub> RECEPTOR AGONISTS IN RHESUS MONKEYS.**

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**Aims:** Selective 5-HT reuptake inhibitors (SSRIs) are used in combination with other drugs to treat chronic pain. Although depression often accompanies chronic pain, SSRIs might alleviate pain independent of the effects on depressive symptoms. By blocking the reuptake of 5-HT, SSRIs indirectly activate multiple 5-HT receptor subtypes.

**Methods:** This study investigated the role of two 5-HT receptor subtypes (5-HT<sub>1A</sub> and 5-HT<sub>2A</sub>) in modifying the antinociceptive and discriminative stimulus effects of morphine in rhesus monkeys.

**Results:** In a warm water tail withdrawal procedure, morphine dose dependently increased the latency of monkeys to remove tails from 50 or 55 °C water. The 5-HT<sub>2A</sub> receptor agonists DOM, quipazine and 2C-T-7 each shifted the morphine dose response curve leftward. This enhancement of the antinociceptive effects of morphine was blocked by a selective 5-HT<sub>2A</sub> receptor antagonist MDL100907. The 5-HT<sub>1A</sub> receptor agonists F13714, 8-OH-DPAT and buspirone did not modify the antinociceptive effects of morphine. In monkeys discriminating 1.78 mg/kg morphine, the 5-HT<sub>2A</sub> receptor agonists DOM, quipazine and 2C-T-7 shifted the morphine discrimination dose response curve rightward and this attenuation was reversed by MDL100907. Neither F13714, 8-OH-DPAT or buspirone modified the discriminative stimulus effects of morphine. Thus, 5-HT<sub>2A</sub> and not 5-HT<sub>1A</sub> receptor agonists enhance the antinociceptive effects of morphine and, at the same doses, attenuate the discriminative stimulus effects of morphine.

**Conclusions:** Collectively, these data suggest that 5-HT<sub>2A</sub> receptors could play an important role in the antinociceptive effects of SSRIs and that the combination of a 5-HT<sub>2A</sub> receptor agonist and morphine might be especially useful for treating pain.

**Support:** Supported by USPHS grants DA 05018 and DA 17918 to CPF and the NIDA and NIAAA intramural research programs.

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**STEREOSPECIFICITY, OR LACK THEREOF, IN HUMAN METHAMPHETAMINE METABOLIC PATHWAYS.**

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**Aims:** There are 2 stereoisomers of methamphetamine (MA), d-MA and l-MA; d-MA is the isomer that is usually abused. In humans MA is metabolized by aromatic hydroxylation and N-demethylation with formation of two major metabolites: para hydroxymethamphetamine (pOH-MA) and amphetamine (AMP). Toxicologists frequently measure pOH-MA but the percentage of the dose converted to pOH-MA metabolites in humans is not well characterized. In this study we examined the dose and enantiomer specific formation of the pOH-MA metabolites.

**Methods:** In this 12-subject, 6-session, double-blind, placebo-controlled, balanced, crossover design study the formation of MA metabolites pOH-MA and AMP were determined in urine after IV dose of d-MA 0.25 and 0.5 mg/kg, l-MA 0.25 and 0.5 mg/kg, racemic MA 0.5 mg/kg, or placebo. Parent drug and metabolite levels were measured by GC-MS and data were analyzed by SPSS.

**Results:** A ~3-fold enantiospecific difference in elimination was seen for AMP formation, with 7% of the dose converted to d-AMP vs. 2% to l-AMP ( $P < 0.001$ ). Correspondingly, d-MA excretion was less than l-MA (42% vs 52%;  $P = 0.03$ ). In contrast to AMP, no differences were seen in formation of d-pOH-MA and l-pOH-MA (11% vs 8%;  $P = 0.94$ ). Although no statistical differences were seen, d-MA elimination may be dose dependent: 48% of the 0.25 mg/kg dose was eliminated as d-MA vs 40% after 0.5 mg/kg and 37% after racemic MA. Similar trends were not seen for l-MA.

**Conclusions:** The formation of AMP metabolites is enantiospecific but the pOH-MA metabolites are not, suggesting that urine pOH-MA may be a more stable biomarker of MA abuse than either urinary MA or AMP. A larger percentage of MA is converted to p-OH-MA (8-11%) than AMP (2-7%), further supporting the utility of using p-OH-MA as a marker of MA abuse.

**Support:** DA18179, DA12521 and RR00079

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**METHODS FOR ASSESSING THE CUMULATIVE TREATMENT EFFECT ON SUBSEQUENT DRUG USE ABSTINENCE.**

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**Aims:** To apply and illustrate new statistical methods, dynamic structural equation modeling (SEM) and marginal structural modeling (MSM), for better assessment of the cumulative treatment effect.

**Methods:** The dynamic selection bias is common in the observational drug abuse data because drug users often selectively enter or quit treatments and form different treatment patterns over time. Currently, the effect of cumulative treatments is mainly investigated by some conventional methods, such as ANCOVA, propensity score adjustment and conventional SEM, which basically ignore the dynamic selection bias over time. Our new methods, which are largely ignored in drug abuse research, can incorporate the dynamic selection bias and should be more appropriate from theoretical and substantive perspectives than the conventional methods for the investigation of the cumulative treatment effect.

**Results:** Natural history data covering 15 years is used for comparison. The effects of cumulative treatments over the first ten years on subsequent abstinence, measured by the number of months with (1) continuous drug use abstinence counted backwards from the end of 15th year and (2) drug use abstinence between the 11th and 15th year, are estimated using the five methods mentioned above. The three conventional methods consistently show a significant cumulative treatment effect on outcome measure 1 but not on measure 2. The dynamic SEM fails to detect any significant effect. The MSM finds the significant effect on both measures.

**Conclusions:** Three conventional methods, even with theoretical drawbacks, may give some hints on the cumulative treatment effect. Although sound theoretically, the dynamic SEM will be problematic in practice, especially when more time points and treatment-related processes for adjustment are involved. In contrast, the MSM is less prone to those problems while maintains the advantages over the conventional methods.

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### NEURONAL CORRELATES OF ORAL ZOLPIDEM ADMINISTRATION: MAGNETIC RESONANCE IMAGING STUDIES IN HEALTHY VOLUNTEERS.

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**Aims:** Zolpidem is a non-benzodiazepine (BZ) sedative/hypnotic that acts preferentially at GABAA receptors containing an  $\alpha 1$  subunit in order to influence inhibitory neurotransmission throughout the central nervous system. Zolpidem's selective pharmacology is believed to underlie its superior ability to treat insomnia with purported reduced abuse liability compared to BZs. Although a great deal is known about the behavioral effects of zolpidem, little is known about its specific effects within the brain. The goal of this multidisciplinary research program is to blend behavioral and receptor pharmacology with brain imaging techniques to probe the neuronal mechanisms that may underlie drug action. More specifically, studies are aimed at understanding the inconsistencies between zolpidem's pharmacological profile and emerging reports in the literature about its abuse potential.

**Methods:** Toward that end, one ongoing study employing functional magnetic resonance imaging (fMRI) following acute oral administration of zolpidem is investigating the dose-response effects of zolpidem on the blood oxygen level-dependent (BOLD) signal during rest, visual stimulation, and reaction time tasks. Results will guide future studies by determining the extent to which the BOLD signal changes with drug and how meaningful those changes are with respect to zolpidem's effect on physiology vs. neuronal activity. The next study will attempt to correlate more comprehensively zolpidem-induced neuronal activity to its behavioral effects.

**Conclusions:** Together, these studies will provide important information about the mechanisms underlying the sedative-like, dysphoric-like, anxiolytic, and reinforcing effects of zolpidem, as well as BZs in general.

**Support:** NIDA grants K01 DA023659 and K05 DA000343.

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### RESILIENCE TO ADOLESCENT BEHAVIORAL RISK AFTER INTRAUTERINE COCAINE EXPOSURE.

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**Aims:** Elucidating post-natal factors which may buffer the emergence of risky behavior in adolescence following intrauterine cocaine exposure (IUCE) can guide public policies and advice to caregivers. We tested whether IUCE increases behavioral risks in early adolescence and identified potential buffering factors.

**Methods:** In a prospective masked longitudinal study of 138 adolescents, the level of IUCE (identified at birth by maternal interview and meconium assay), was compared to a composite indicator of behavioral resilience - no HIV risk behaviors, <3 delinquent acts, no substance initiation by audio computer assisted self interview and urine assays. Covariates included: incarcerated parent, whether caregiver was birth mother, kin or unrelated, exposure to violence ages 8-14, and caregivers level of supervision.

**Results:** Sample characteristics: 88% Black, 49% female, mean age 14.2 (sd  $\pm$ .7) years, 46% no IUCE, 36% lighter IUCE, 18% heavier IUCE. In bivariate analyses, 59% of those with no IUCE were behaviorally resilient, as were 52% lighter IUCE, and 36% heavier IUCE (global  $p=0.16$ ; no IUCE vs. heavier IUCE, crude OR=2.53,  $p=0.054$ ). In multivariate logistic regression, controlling for caregiver identity and parental incarceration did not change relationship of IUCE with resilience. Top quartile of caregiver supervision vs. all other quartiles and lower 3 quartiles of exposure to violence vs. top quartile were associated with greater adjusted odds of behavioral resilience (AOR 5.87, 95% CI 2.01-17.12,  $p=.001$  and AOR 3.15, 95% CI 1.47-6.76,  $p=.003$ , respectively). When these factors were included in the analysis, the effects of no IUCE vs heavier IUCE on resilience were unchanged (AOR 2.56, 95% CI .88-7.43,  $p=.08$ ). Analyses evaluating composite prenatal exposure to tobacco, alcohol, marijuana, and cocaine showed similar buffering effects.

**Conclusions:** Less exposure to violence throughout childhood and stricter adult supervision in adolescence increase behavioral resilience in young adolescents, regardless of the level of prenatal cocaine exposure.

**Support:** RO1 DA06532 and MO1 RR00533

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### AN EXPLORATORY QUALITATIVE STUDY ON DISEASE MODELS AND PERCEPTIONS TOWARDS CANNABIS USE AMONG PATIENTS WITH SCHIZOPHRENIA.

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**Aims:** To explore disease models of cannabis using patients with schizophrenia, to further evaluate reasons for cannabis use, and to clarify whether patients report a causal link between cannabis use and schizophrenia

**Methods:** Ten consecutive patients fulfilling criteria for schizophrenia and for a harmful use of/dependence from cannabis (ICD-10 F20.0 + F12.1 or F12.2) were recruited from the in- and outpatient clinic of the Psychiatric University Hospital Zurich and interviewed using qualitative methodology.

Furthermore information on amount, frequency and effects of use was obtained. Exclusion criteria were insufficient language skills, acute psychosis, acute intoxication and personality disorders.

**Results:** None of the patients described a causal link between use of cannabis and schizophrenia. Explanatory models included upbringing under difficult circumstances (5) or use of substances other than cannabis e.g. hallucinogens (3). Two patients gave other reasons. Four patients regarded cannabis as a valid therapeutic aid and reported that positive aspects (reduction of anxiety and tension) prevailed its possible disadvantages (exacerbation of positive symptoms).

**Conclusions:** In this small sample, patients with schizophrenia had a rather positive view of cannabis and used it (specifically) to reduce tension, to attenuate symptoms of depression or (simply) for relaxation purposes. This perception was reflected in individual models of illness, which negated a causal link between schizophrenia and use of cannabis. With respect to therapeutic adherence, we suggest that clinicians consider these findings in their work with patients suffering from these comorbidities.

**Support:** This work did not receive any financial support.

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### THE SUBSTITUTION PROFILE OF THE CANNABINOID AGONIST NABILONE IN HUMAN SUBJECTS DISCRIMINATING $\Delta 9$ -THC.

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**Aims:** The central effects of the primary active constituent of cannabis,  $\Delta 9$ -THC, appear to be exerted through cannabinoid receptors. However, due to the limited availability of pharmacological agents acting on the endogenous cannabinoid system that are approved for use in humans, clinical research in this area is incomplete. The purpose of this study is to demonstrate the role of cannabinoid receptors in the effects of  $\Delta 9$ -THC in humans.

**Methods:** The primary outcome for this study is the discriminative stimulus produced by  $\Delta 9$ -THC, measured using the drug-discrimination procedure, which can be used to characterize the pharmacological profiles of a drug. In addition, several other measures are collected to determine a profile of  $\Delta 9$ -THC effects, including physiological indices, self-report questionnaires, the Multiple-Choice Procedure to assess drug reinforcement, a time reproduction procedure, as well as memory and psychomotor performance tasks. Initially, healthy subjects who report moderate cannabis use, but do not meet criteria for cannabis dependence, learn to discriminate 25 mg  $\Delta 9$ -THC. Next, placebo and doses of  $\Delta 9$ -THC (5, 7.5, 15 and 25) and the cannabinoid agonist nabilone (1, 2, 3 and 5 mg) are tested. Methylphenidate (5, 10, 20 and 30 mg) is also included as a negative control. Data will be analyzed using repeated-measures ANOVA.

**Results:** The training dose of  $\Delta 9$ -THC functioned as a discriminative-stimulus and produced prototypical cannabinomimetic effects (e.g., increased positive subject ratings and heart rate). Nabilone, but not methylphenidate, dose dependently substituted for the training dose of  $\Delta 9$ -THC and produced behavioral and physiological effects that overlapped with  $\Delta 9$ -THC.

**Conclusions:** These results support preclinical data indicating that the discriminative-stimulus effects of  $\Delta 9$ -THC are mediated through endogenous cannabinoid systems.

**Support:** This research is supported by grants from the National Institute on Drug Abuse (K01 DA018772) to Dr. Joshua A. Lile, a Center for Biomedical Research Excellence (P20 RR015592) and a General Clinical Research Center (M01 RR002602).

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**LEGAL ISSUES AMONG DRUG-USING PREGNANT WOMEN.**

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**Aims:** While many drug-using pregnant women have legal involvement (Daley et al., 2000), the extent to which these women represent a unique sub-group needing specialized treatment is unknown. As a first step, the characteristics associated with legal involvement in drug-using pregnant women were examined.

**Methods:** Pregnant women (N=995) were screened for possible MOTHER study admission, a multi-site randomized controlled trial (RCT) for opioid-dependence during pregnancy. All participants completed a standardized screening questionnaire. Women on probation, parole, or with an impending charge/trial were classified as legally involved (n=236; 24% of total) and were compared to women reporting no legal involvement (n=759; 76% of total) on all screening variables.

**Results:** Fewer legally involved women reported current employment (8% vs. 12%, p<.05). Legally involved women reported more current use of opioids and cocaine (90% vs. 81% and 52% vs. 40%, respectively; p's <.01), more episodes of prior opioid treatment (4.4 vs. 3.2, p<.01) and were more often methadone-maintained (83% vs. 75%, p<.05). In terms of RCT eligibility, more of the legally involved women were excluded from the study (60% vs. 48%, p<.01), although only a quarter of these women were excluded due to their legal involvement. Other reasons for exclusion among legally involved pregnant women included benzodiazepine use (17%), a medical condition that precluded participation (10%), or alcohol use/abuse (8%).

**Conclusions:** Results suggest that drug-using pregnant women involved in the criminal justice system have more severe drug use and some other co-occurring problems. Final MOTHER study data will allow examinations of the implications of legal involvement on treatment outcome in opioid-dependent pregnant women.

**Support:** NIDA R01DA18410, 15764, 18417, 15738, 15832, 17513, 15778, & 15741

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**A CLINICAL TRIAL COMPARISON OF TWO FORMULATIONS OF DEPOT BUPRENORPHINE FOR PAIN.**

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**Aims:** Opioid medications are the most effective analgesics but side effects and the potential for developing tolerance and dependence may make physicians hesitant to prescribe them. Recent preclinical studies suggest that the combination of opioid medications with ultra-low doses of opioid antagonists enhances the potency of the opioid while reducing side effects, including the development of tolerance and dependence. Results of limited clinical research, however, have yielded inconsistent results. The main goal of this study is to determine whether the addition of an ultra-low dose of naloxone, an opioid antagonist, to buprenorphine, an opioid analgesic medication, increases analgesic potency and reduces side effects compared to buprenorphine alone.

**Methods:** A total of 12 participants with moderate levels of pain (4-7 in pain intensity on a scale of 0-10) will be randomly assigned to treatment order before being given study drugs in a double-blind crossover design. Participants are given 5 doses of one of two medication regimens: IV buprenorphine+ultra-low-dose naloxone, or IV buprenorphine alone within a 2-week period. After a 1-week inter-trial interval, participants are crossed over to the second treatment condition for 5 additional doses administered within a 2-week period. The entire study duration will range from 3 to 5 weeks, depending on the dosing schedule. Each study day, participants will provide a daily pain assessment, receive administration of study medication, and will then be monitored and assessed for pain and side effects over the next six hours.

**Conclusions:** This important study will provide results of pain intensity and self-reported side effects/adverse events. The current presentation includes a detailed description of the study design, participant eligibility criteria, assessment measures, and study flow.

**Support:** This study is funded Reckitt-Benckiser, agreement #20080605.

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**COCAINE DEPENDENCE AND CONCURRENT MARIJUANA USE: A COMPARISON OF CLINICAL CHARACTERISTICS.**

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**Aims:** Marijuana is the most commonly used illicit substance in the general population and among cocaine users. Rates of use among clinical samples of cocaine dependent patients range from 59 to 89%. This study assessed marijuana use in 1183 individuals seeking outpatient treatment for cocaine dependence and its potential impact on the clinical profile at baseline.

**Methods:** Based on past 30 days of use, the sample was divided into three groups: (1) patients reporting no recent marijuana use (n=634); (2) occasional use (n=403); (3) and frequent concurrent marijuana use (n=146). Differences on measures of substance use, addiction severity, psychopathology, and sociodemographics were examined across levels of marijuana use.

**Results:** Frequent marijuana users were more likely to be female, Caucasian, and younger than other groups. Frequent marijuana users were heavier users of cocaine and alcohol, and had more severe medical, legal, and psychiatric problems, including antisocial personality disorder than occasional or non-users of marijuana.

**Conclusions:** This type of drug use, while not exclusionary in most cocaine clinical trials, may introduce an important source of population heterogeneity to consider in evaluation of treatment response. Together, these findings suggest that concurrent and frequent marijuana use in cocaine dependent patients is associated with more severe psychosocial impairment and may require more intensive or different treatment. Accounting for this heterogeneity in the cocaine dependent population may improve treatment outcome.

**Support:** NIDA P50 DA009262

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**REINSTATEMENT OF NICOTINE-SEEKING BEHAVIOR IN RATS: EFFECTS OF NICOTINE CUES, PRIMING, STRESS, AND THEIR COMBINATION.**

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**Aims:** Drug cues, priming, and stress have been thought of as the major risk factors contributing to relapse in abstinent subjects. Recent animal studies have demonstrated that nicotine cues reliably reinstate nicotine-seeking behavior. However, investigation of the effects of nicotine priming and stress exposure as well as their combination with nicotine cues is limited. This study, using a response-reinstatement procedure, examined the motivational effects of a nicotine-associated cue, nicotine priming, pharmacological stress, and combination of the cue with priming or stress.

**Methods:** Male Sprague-Dawley rats were trained in 30 daily 1-h sessions to intravenously self-administer nicotine (0.03 mg/kg/infusion, free base) on an FR5 schedule and associate a cue with each nicotine administration. Then, lever responding was extinguished by saline substitution of nicotine and omission of the cue. After rats reached an extinction criterion, reinstatement tests were conducted under five conditions: cue, priming, stress, cue+priming, and cue+stress.

**Results:** Nicotine (0.25 mg/kg, s.c.) priming, stress (yohimbine, 2 mg/kg, i.p.), and response-contingent re-presentation of the cue significantly reinstated the extinguished nicotine-seeking behavior with cue producing the most robust effect. Combination of cue with either priming or stress did not produce stronger effect than cue alone.

**Conclusions:** These results confirm the motivational effects of nicotine cue, priming, and stress in the present animal model of relapse and demonstrate the most robust ability of cue exposure to elicit nicotine-seeking after extinction. The present findings suggest that re-exposure to smoking-related environmental cues may play a critical role in the high recidivism rates of smoking and thereby lend support for the continued effort on cue management as a strategy for the treatment and prevention of smoking relapse.

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### THE RELATIONSHIP BETWEEN THE RESPONSIVITY TO COCAINE-RELATED STIMULI AND OTHER COGNITIVE PERFORMANCE.

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**Aims:** Cocaine users exhibit an attentional bias for drug-related stimuli and are more impulsive in different cognitive tasks than controls. However, the relationship between the responsivity to cocaine-related stimuli and the performance on other cognitive tasks is not well explored.

**Methods:** We compared the performance of cocaine-dependent and control subjects on a cocaine word-based emotional Stroop task, probabilistic reversal learning task and two different measures of impulsivity: response inhibition and delay discounting. We specifically analyzed the relationship between the response time to cocaine vs. neutral words in the Stroop task and performance on response inhibition (immediate memory task), delay discounting and probabilistic reversal learning.

**Results:** Our preliminary data show that response time difference (cocaine words – neutral words) of cocaine-dependent subjects ( $n = 11$ ) in Stroop task was significantly larger than that of controls ( $n=12$ ;  $p < 0.05$ ). This response time difference was positively correlated with the number of incorrect responses on the reversal learning task ( $P < 0.05$ ), but not with response inhibition or delay discounting.

**Conclusions:** The significant correlation between Stroop and reversal learning performance, but not with performance on tests of impulsivity provides preliminary evidence that attentional bias and reversal learning (compulsiveness) may be independent from response inhibition and temporal discounting (impulsivity); though both are prominent features of cocaine dependence.

**Support:** DA024157, DA009262

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### A RANDOMIZED CONTROLLED TRIAL ON NALTREXONE IMPLANTS AND METHADONE MAINTENANCE AMONG HEROIN-DEPENDENT INMATES: RESULTS 6 MONTHS AFTER PRISON RELEASE.

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**Aims:** Heroin-involved offenders have limited access to methadone maintenance (MMT) while incarcerated. Risk of relapse and overdose death after release are high. MMT reduces heroin use, mortality and crime and is increasingly made available in prisons. Naltrexone is an opioid-receptor antagonist, blocking the rewarding effects of heroin without inducing dependence. Naltrexone implants provide opioid blockade for 6 months and reduce heroin use and mortality. This is the first trial comparing naltrexone implant treatment with MMT to prevent heroin relapse after prison release.

**Methods:** This study was an open-label, two-arm, naturalistic, randomized-controlled trial. Main inclusion criterion was heroin dependence prior to current incarceration. Treatment was initiated on average 1 month before prison release. First follow-up was scheduled at 6 months after release when group crossover was optional.

**Results:** The sample comprised 46 poly-drug using inmates of which 27 initiated treatment before release: Sixteen of 24 in the naltrexone implant group and 11 of 22 in the MMT group. The intention-to-treat analysis was conducted on the whole sample, independent of treatment initiation. It showed a significant reduction in heroin use and criminal activity 6 months after release. These findings were supported by the completer analysis. In our sample, naltrexone implant treatment showed a significantly higher compliance rate than MMT.

**Conclusions:** Naltrexone implant treatment was equivalent to MMT in reducing heroin use and criminal activity. Access to MMT should be facilitated in criminal justice settings. Naltrexone implants were considered a valuable treatment option by heroin-involved offenders and warrant further evaluation in criminal justice settings.

**Support:** The Research Council of Norway

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### ADOLESCENT TOBACCO INITIATION, USE AND ONGOING NICOTINE ADDICTION: PERSPECTIVES ON A REDUCED NICOTINE CONTENT POLICY.

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**Aims:** Nicotine addiction, the cause of 50% premature mortality in continuing users, is high among adolescents. Unlike adults whose issues are more linked to cessation/relapse, adolescents are exposed to initiation, facilitation and early smoking maintenance leading to nicotine addiction. Efforts to develop effective interventions to prevent initiation of tobacco use and treat addiction in young people are vital; youth have been targets of tobacco industry marketing. We discuss a combined developmental and behavioral model to illustrate the multi-dimensional impact of a Reduced Nicotine Content cigarette (RNC) policy on youth smoking and its implications for modifying smoking intention, initiation, maintenance and addiction among adolescents.

**Results:** RNC might decrease smoking initiation, addictiveness, relapse and cessation. Biological and psychological vulnerabilities, exposure, trajectory and motivation to smoke are considered. To minimize risk of unintended consequences (attenuation of harm perception, trajectory variants, increase in tobacco constituent harm, and altered industry marketing approaches), it would need to be initiated as an integrated component of tobacco control policy. Caveats include generalizability of adult research to adolescents and require standardizing smoking assessments to adolescents.

**Conclusions:** Disparate effects of tobacco on adolescents are multi-factorial, including vulnerability to tobacco addiction, developmental factors that cause susceptibility to market campaigns or tobacco product modifications, accessible interventions to support smoking cessation through treatment of nicotine dependence/withdrawal. To rationally anticipate effects of a RNC policy on adolescents, an integrative disparities research model is needed. Threshold levels of nicotine effect and addiction are theoretical concepts that require further evaluation. Additional adolescent research is suggested in topography, pharmacodynamics, pharmacokinetics, delivery, and their impact on smoking trajectory.

**Support:** DHHS, NIH, NIDA-IRP Baltimore MD

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### PHARMACOKINETICS OF CRUSHED INTRANASAL OXYCONTIN® IN NON-DEPENDENT PRESCRIPTION OPIOID USERS.

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**Aims:** Intranasal (IN) prescription opioid abuse is common. The purpose was to evaluate the pharmacokinetics of IN Oxycontin® (OC).

**Methods:** Healthy adults abusing opioids enrolled in this within-subject, placebo-controlled double-blind, randomized, inpatient study. Four dose conditions were examined in separate sessions: three volume-matched IN crushed OC doses [placebo (lactose), 15 & 30 mg/70 kg] and one IV oxycodone (5 mg/70 kg) dose. Serial blood samples were collected before and for 24 h after drug administration along with 24-h urine collection. Oxycodone, noroxycodone and oxymorphone were determined using validated liquid chromatography-electrospray ionization-tandem mass spectrometric methods with deuterated analogs for internal standard. The lower limit of quantitation was 0.2-0.4 ng/mL for plasma and 10 ng/mL for urine.

**Results:** Plasma oxycodone was detectable within 5 min after insufflation with a Tmax of 38 min for the low OC dose and 72 min for the high OC dose. Oxycodone Cmax was 31.9 and 55.7 ng/mL for the low and high OC doses, respectively. Bioavailability for both IN OC doses was similar (mean: 79.4%, range: 58.7-100%). The primary plasma metabolite was noroxycodone. Oxymorphone also was present. Within 24-h, 31.5% of the high IN dose was excreted in the urine; 17.1% as oxymorphone, 6.5% as oxycodone and 7.8% as noroxycodone. Oxycodone and noroxycodone were excreted primarily as unconjugated, while oxymorphone was excreted as conjugated.

**Conclusions:** Crushing OC is an effective means of bypassing the extended release coating as evidenced by the rapid entry of oxycodone into the bloodstream with peak concentrations within 1 h. Previous reports indicate the oral bioavailability of OC is 60%; however, the intranasal route produced nearly 80% bioavailability indicating it is a more efficient route for diversion. The pharmacokinetic profile of snorted crushed OC indicates substantial abuse liability.

**Support:** NIDA R01 DA016718 and K12 DA14040

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**REPEATED METHAMPHETAMINE ALTERS PREFRONTAL CORTEX NEUROTRANSMISSION.**

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**Aims:** Long-term methamphetamine (METH) use is associated with a loss of cognitive inhibitory control in human subjects, which is linked to anomalies in prefrontal cortex (PFC) activity. As the molecular underpinnings of METH-induced changes in PFC function remain unclear, we aimed to examine the neurochemical and proteomic changes in PFC produced by repeated exposure to low dose, non-toxic, METH.

**Methods:** C57BL/6J mice were pretreated with either METH (10 x 2mg/kg) or saline, and changes in indices of PFC glutamate and dopamine transmission were examined using conventional and no-net flux in vivo microdialysis, as well as immunoblotting, following 24 hours or 3 weeks withdrawal.

**Results:** An acute challenge with 1mg/kg METH elevated dopamine, but not glutamate, in the PFC. In contrast, repeated METH treatment produced a large sensitized response in both dopamine and glutamate at both time-points. Repeated METH failed to alter PFC basal glutamate content or to affect the expression of any of the glutamate receptor-associated proteins examined. However, repeated METH elicited a number of dopamine-related changes in the PFC including: elevated basal content, a reduction in probe clearance and, surprisingly, an increase in DAT expression.

**Conclusions:** Together, these data illustrate the potential for the repeated administration of non-toxic doses of METH to produce enduring neuroplasticity within PFC dopamine and glutamate systems. Based on the data to date, it would appear that a repeated low-dose METH elicits a dysfunction in DAT regulation of PFC dopamine levels, which may underlie the cognitive abnormalities associated with repeated drug use.

**Support:** Funding provided by a Young Investigator's Award to KKS.

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**FEELING AND PERFORMING BETTER FOLLOWING PLACEBO METHYLPHENIDATE: THE ROLE OF EXPECTANCY.**

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**Aims:** Prescription stimulant misuse has increased over the past decade and has reached alarming rates among college-aged students. Common motivations for use include improving concentration, enhancing alertness, and feeling high. The efficacy of drugs like methylphenidate (MPH) in enhancing cognitive performance and subjective arousal is inconclusive, and it is possible that these effects may arise from expectancy rather than pharmacology.

**Methods:** To examine this, 13 MPH-naïve college students (69% male) completed a battery of cognitive tests and measures of subjective arousal under 2 conditions: (1)ingesting what they believed to be MPH (actually placebo), and (2)ingesting no medication. Study sessions were 2 weeks apart and the order of the conditions was counterbalanced.

**Results:** When participants believed they had ingested MPH, they reported expecting to perform better ( $t=2.28$ ,  $p<.05$ ,  $d=.91$ ) and feeling more high ( $t=2.38$ ,  $p<.05$ ,  $d=1.15$ ), with a trend toward feeling more stimulated ( $t=2.13$ ,  $p=.055$ ,  $d=.87$ ) and having more energy and intellectual efficiency ( $t=1.91$ ,  $p=.08$ ,  $d=.76$ ). Improved attention and vigilance on the Conners' Continuous Performance Test was also found when subjects expected MPH. Participants had a higher nonclinical confidence index ( $t=4.01$ ,  $p<.05$ ,  $d=1.71$ ), fewer commissions ( $t=-2.16$ ,  $p=.05$ ,  $d=-.85$ ), and better response time consistency ( $t=2.21$ ,  $p<.05$ ,  $d=1.43$ ). Conversely, when participants expected MPH, there was a trend toward impaired memory on the California Verbal Learning Test total word recall ( $t=-2.06$ ,  $p=.06$ ,  $d=-.81$ ).

**Conclusions:** Results indicate that expectation alone to receive MPH can enhance subjective arousal and cognitive ability, especially attention. Interestingly, memory declined when subjects expected MPH. Perhaps when expecting the drug, participants put forth less conscious effort. Alternatively, they may have expected improved attention, but not memory. Challenging the expectancies that individuals hold for prescription stimulants, and separating the psychological and pharmacological effects of these drugs, may prove effective in reducing misuse.

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**FACTORS OF DRUG ABUSE FOR BLACK AND CARIBBEAN EMERGING ADULTS.**

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**Aims:** The overall aim of this study was to discover the factors related to self-reported drug abuse for Black and Caribbean American emerging adults by conducting secondary data analyses using the National Survey of American Life. There is still a gap in the literature concerning the prevalence of substance use and abuse among non-white emerging adult samples. However, previous research suggests that a combination of sociodemographic and psychosocial variables may predict substance use. The specific aim of the current research was to investigate how gender, discrimination, psychological well-being, perceived neighborhood characteristics and economic hardships in combination predicated drug abuse history.

**Methods:** The data of 641 Black and Caribbean American emerging adults (ages 18 -25) who participated in the National Survey of American Life were used in these analyses. Approximately five percent of the community-based sample reported having a history of drug abuse. Drug abuse history was determined using DSM-IV criteria and was then transformed into the dichotomous variable indicating whether there was a drug abuse history or not. Based on the results of bivariate analyses a logistic regression model was analyzed using the entry method.

**Results:** Preliminary findings suggest that gender, perceived neighborhood crime, seriousness of drugs in the neighborhood, at least one depressive moment, and the cumulative experience of daily discrimination are related to drug abuse. The initial results from the logistic regression reveal that it is the combined influence of gender, daily discrimination, and reporting at least one depressive moment that predict the likelihood that someone will have an experience with drug abuse by the time they are an emerging adult.

**Conclusions:** According to the preliminary results, Black and Caribbean males that have struggled with depression, regardless of the amount of daily discrimination they encounter are more at risk for drug abuse prior to adulthood. The potential interaction between gender and discrimination needs further exploration.

**Support:** T32-DA0 7233-25

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**BUPRENORPHINE DETOXIFICATION: EFFECTS ON PROBLEM SEVERITY AND AIDS RISK BEHAVIORS.**

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**Aims:** To assess the effects on ratings of problem severity and AIDS risk perceptions and behaviors of a 30-day buprenorphine detox.

**Methods:** In association with a study of early engagement strategies among opioid-addicted individuals ( $n = 239$ ; 55% male; 92% African American) entering a 30-day buprenorphine detox, data were collected at baseline and at the end of the detox. Participant's ratings of the severity of Drug, Alcohol, Medical, Legal, Employment, Family/Social, and Psychiatric problems were assessed using the Addiction Severity Index. AIDS risk perceptions and behaviors were assessed using the Texas Christian University AIDS Risk Assessment.

**Results:** Significant reductions from baseline to end of detox were found for Drug ( $M = .21$  v.  $.047$  respectively), Alcohol ( $M = .051$  v.  $.014$  respectively), Legal ( $M = .159$  v.  $.059$  respectively), and Psychiatric ( $M = .038$  v.  $.012$  respectively) problem severity ratings. Results also revealed a significant reduction from baseline to end of detox in the number of times, on average, that participants reported injecting drugs during the previous 30 days. Participants' beliefs regarding their risk of contracting AIDS and their need and intent to engage in risk reduction behaviors also changed from baseline to end of detox. Specifically, participants reported an increased perception of their risk of contracting AIDS and an increased intent to change drug use behaviors in order to reduce their AIDS risk.

**Conclusions:** Despite research suggesting that detox is ineffective as a stand-alone treatment for opioid-addicted clients, current findings suggest significant short-term reductions in several client problem areas. In addition, there is indication that involvement in even brief treatment is associated with an increased awareness regarding AIDS risk and increased intent to reduce the level of that risk.

**Support:** This research was funded by NIDA grant RO1 DA 11402. We also thank Reckitt Benckiser for their generous support of this project.



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**INCIDENCE OF DRUG USE AMONG SCHOOL ADOLESCENTS IN BOGOTÁ, COLOMBIA.**

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**Aims:** As one of the world's leading cocaine producers, most of the attention to the drug problem in Colombia has focused on international trafficking, and little on the epidemiology of use and the assessment of the risk of drug use onset. This study estimates incidence of marijuana, cocaine, ecstasy, coca-paste and inhalants use (drug use) and explores factors associated with use onset, in a representative sample of school-attending adolescents in Bogotá, Colombia.

**Methods:** A longitudinal study was carried out among 2279 8th–10th grade students (Wave1) in 23 schools in Bogotá, selected in a stratified multistage probability cluster sample. This sample was followed for one year to determine the incidence of drug use.

**Results:** The average age of participants at Wave1 was 14.8 years (SD=1.2); 50% of the sample was male, 67% studied in public schools and 56% belonged to the lowest socio-economic strata (SES). Nearly one-fifth (19%) reported ever having used drugs by Wave1. Wave2 data was obtained from 73% (N=1350) of students who had not used drugs by Wave1. Initiation of drug use (mostly marijuana) was reported by 5.7% of the Wave2 sample. After controlling for the effects of age, gender, SES, school type and drug-use attitudes, the strongest predictors of initiation were having smoked tobacco (Adjusted Odds Ratio [AOR]=3.8, 95% Confidence Interval [CI]=2.0,7.2), drug-using peers (AOR=3.5, CI=2.1,6.1), a high degree of problematic behavior (AOR=3.1, CI=1.6,5.8) and binge drinking (AOR=2.8, CI=1.6,4.9).

**Conclusions:** Based on these results, over 12000 8th–10th grade students in Bogotá schools are predicted to initiate drug use within the next year. It is estimated, based on data from the USA, that up to 18% of initiators are at risk of developing drug abuse/dependence. This first longitudinal study of the risk of drug use onset among students in Colombia provides useful information for developing behavioral-life-skills prevention strategies, particularly for youth using legal drugs or those in circles where drug use is a normalized behavior.

**Support:** Milstein Foundation scholarship for doctoral studies (to CL-Q)

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**PROVIDER CONFIDENCE RECOGNIZING OPIOID ANALGESIC ABUSE IN HIV CARE SETTINGS.**P. Lum<sup>1</sup>, S Little<sup>2</sup>, D Hersh<sup>2</sup>, R Thawley<sup>1</sup>, J Egan<sup>3</sup>, J Mitty<sup>4</sup>, D Fiellin<sup>5</sup>; <sup>1</sup>University of California, San Francisco, CA, <sup>2</sup>San Francisco Department of Public Health, San Francisco, CA, <sup>3</sup>New York Academy of Medicine, New York, NY, <sup>4</sup>Brown University, Providence, RI, <sup>5</sup>Yale University, New Haven, CT

**Aims:** Our aim was to assess HIV providers' confidence in recognizing OAA. Pain syndromes are common in HIV+ patients, who also are affected commonly by opioid use disorders. While opioids can treat pain effectively, prescribers must consider the adverse consequences of missed addiction diagnoses.

**Methods:** HIV providers prescribing opioids for chronic pain were recruited from 10 national sites participating in a HRSA-funded buprenorphine initiative. In an anonymous online survey, we asked about provider demographics and experience, patient characteristics, and provider attitudes and practices regarding chronic pain and addiction. Confidence was assessed by a 10-point analog scale (0=not at all, 10=extremely confident). We used GLM techniques to examine factors associated with provider confidence in their ability to recognize OAA in HIV+ patients.

**Results:** 106 providers (80 MDs, 19 NPs, 7 PAs) responded; mean age 45–54 yrs, 53% female, 71% white; and an average of 12 years in HIV care and 70 patients per month. Respondents estimated 37% of patients were IDU, 28% had chronic pain, 21% received opioids for pain, and 12% were addicted to prescription opioids. 39 providers prescribed buprenorphine. Provider confidence recognizing OAA was moderate (mean=6.3) and highly correlated with confidence diagnosing and treating chronic pain. Higher confidence recognizing OAA was associated with male sex ( $p=.04$ ), patient volume ( $p<.03$ ), prescribing buprenorphine ( $p=.009$ ), routine discussion of substance use issues ( $p=.03$ ), urine toxicology screening ( $p=.01$ ), urine toxicology when misuse is suspected ( $p=.002$ ), and prescribing longer-acting opioids ( $p=.001$ ).

**Conclusions:** HIV providers have limited confidence in recognizing OAA. Clinical practices designed to reduce misuse and increase early detection and treatment of opioid dependence are associated with higher confidence recognizing OAA. Guidelines to improve the quality of opioid prescribing in HIV clinics may aid in the diagnosis of addictive disorders and prevent their adverse outcomes.

**Support:** HRSA H97HA03799

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**KUDZU EXTRACT TREATMENT DOES NOT INCREASE THE INTOXICATING EFFECTS OF ALCOHOL IN HUMAN VOLUNTEERS.**

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**Aims:** Our previous studies of kudzu extract have revealed that it reduces alcohol consumption in both a naturalistic laboratory and outpatient setting. However, the mechanism of its effects on alcohol intake is not well understood. One theory is that kudzu may increase the intensity or duration of the subjective/psychomotor effects of alcohol and delay drinking.

**Methods:** The present study was conducted in 12 healthy adult male and female participants (age  $27.5 \pm 1.89$  years) who reported drinking moderate amounts of alcohol ( $7.8 \pm 0.63$  drinks/week). Individuals signed informed consent to participate in this double-blind, placebo-controlled crossover study of kudzu extract (1 g t.i.d.) versus placebo (counter-balanced). After 7 days of treatment, participants came to the laboratory and were given a challenge dose of alcohol (either 0.35 or 0.7 g/kg) and vital signs, blood alcohol levels, subjective reports of intoxication (via visual analog scales and questionnaires), psychomotor performance and body sway were measured.

**Results:** Kudzu extract failed to alter alcohol-induced changes in heart rate, blood pressure, skin temperature, body sway or continuous performance. In addition, there were no significant effects of kudzu extract on alcohol-induced subjective responses (e.g., alcohol effects, drunk, floating, clumsy or dizzy). Individuals treated with kudzu extract experienced a slightly more rapid rise in plasma alcohol levels, but only after the 0.7 g/kg dose. This transient effect during the first 15 minutes of the ascending plasma alcohol curve lasted only 10–15 minutes; there were no differences in peak plasma alcohol levels or alcohol elimination kinetics.

**Conclusions:** These data suggest that while treatment with kudzu extract results in a reduction in alcohol drinking behavior, the mechanism of this effect is not related to an alteration in alcohol's subjective, physiological or psychomotor performance effects, suggesting that another mechanism, such as altered cue responsiveness and/or craving or desire for alcohol may be responsible.

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**SMOKED MARIJUANA DISCRIMINATION IN HUMANS.**

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**Aims:** Although the drug discrimination model has been widely used to characterize the discriminative stimulus and subjective effects of many drugs of abuse, it has been underrepresented in studies of smoked marijuana.

**Methods:** Five participants who reported recreational marijuana use (1–2 times/wk) were trained to discriminate placebo marijuana and active marijuana cigarettes containing 2.8% THC. During each of two training sessions, participants smoked 3 puffs from placebo and active marijuana cigarettes, each administered twice in randomized order, separated by 4 hrs. The cigarettes were identified by letter codes. During the next three sessions, six trials were conducted with placebo and active marijuana cigarettes each administered three times in randomized order. Thirty minutes after each cigarette, participants were asked to identify the cigarette by letter code.

**Results:** All 5 participants reliably (i.e., 6 of 6 times) discriminated 2.8% THC from placebo cigarettes. Marijuana was identified as marijuana by all participants, and placebo was identified as placebo in all but one trial by one participant. There were significant marijuana-related increases in VAS ratings of "Good Drug Effect," "Strength of Effect," "Like the Effect," and "Desire to Take Drug Again," as well as "Sedated," "High," and "Noises Sound Different." Heart rate and self-reported marijuana craving significantly increased after active marijuana relative to placebo. Finally, participants failed to report differences in physical or sensory characteristics (e.g., taste, harshness of smoke, "draw" or burn rate, appearance) between active and placebo cigarettes.

**Conclusions:** Thus, young adults who report recreational marijuana smoking can be trained to discriminate marijuana from placebo, and it appears they based their drug identification on central or mood effects and not on peripheral or sensory cues. These results suggest that the drug discrimination model with smoked marijuana could be used for medication development in humans.

**Support:** Supported by a Bridge Award from WSU SOM and Joe Young Sr. Funds (State of Michigan).

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### OPIATE HISTORY SENSITIZES DORSAL RAPHE SEROTONIN NEURONS TO GABAERGIC SYNAPTIC INPUTS FOLLOWING STRESS-INDUCED REINSTATEMENT.

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**Aims:** The serotonin (5-hydroxytryptamine, 5-HT) system plays an important role in stress-related psychiatric disorders such as anxiety and depression and has more recently been implicated in substance abuse. The serotonergic dorsal raphe nucleus (DR) is regulated by opiates as well as stressors and stress neurohormones. We hypothesize that the 5-HT DR system is a neurobiological substrate of stress-induced opiate relapse. Specifically, we propose that stressors mimic the effects of opiate withdrawal on 5-HT DR neurons (both inhibit 5-HT neurotransmission), reinstating drug-seeking behaviors.

**Methods:** Swim stress-induced reinstatement of previously extinguished morphine conditioned place preference (CPP) was used to model stress-induced relapse in rats. Immediately following the reinstatement test, rats were sacrificed and brain slices prepared for whole-cell patch-clamp recordings of GABA synaptic activity in 5-HT DR neurons.

**Results:** Following extinction, swim stress reinstated CPP in morphine conditioned but not saline conditioned subjects. Electrophysiology studies show that 5-HT DR neurons in the morphine group had an increased amplitude of spontaneous inhibitory postsynaptic currents (sIPSCs), an indication of greater postsynaptic GABA receptor density and/or sensitivity, compared to saline controls. This effect was not observed in non-5-HT neurons.

**Conclusions:** Previous experiments demonstrated that the stress neurohormone corticotropin-releasing factor enhances GABA synaptic activity in 5-HT DR neurons. Therefore, the current data indicate that previous exposure to morphine may sensitize 5-HT DR neurons to the GABAergic inhibitory effects of stress. This sensitized stress response within the 5-HT DR system may contribute to stress-induced reinstatement of drug-seeking behaviors. These data are important in understanding the role of serotonin in opiate relapse and may lead to novel treatments to prevent opiate relapse.

**Support:** Supported by PHS grant DA 20216 (LK).

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### DISINHIBITION AND REWARD SENSITIVITY IN RELATION TO ALCOHOL CONSUMPTION BY UNIVERSITY UNDERGRADUATES.

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**Aims:** Deficits of prefrontal cortex functioning and associated executive cognitive impairments are well known correlates of chronic alcoholism and may reflect cumulative neurotoxic effects of high alcohol exposure. However, to some extent such associations may also reflect traits predating alcohol exposure which predispose to heavy drinking.

**Methods:** In the present study, 60 university undergraduates aged 18-25 years were administered the Alcohol Use Disorders Identification Test (AUDIT), Frontal Systems Behavior Scale (FrSBe), and Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ). All participants reported they were at least occasional drinkers who rarely or never used illicit drugs and had no reported history of head injury or neurological problems. All were sober at time of testing.

**Results:** AUDIT total scores were significantly positively correlated with FrSBe Disinhibition scores (index of orbitofrontal dysfunction),  $r = .39$ ,  $p < .01$ , and with SPSRQ Reward Sensitivity scores,  $r = .60$ ,  $p < .01$ . The latter were significantly negatively correlated with age at onset of regular drinking,  $r = -.39$ ,  $p < .01$ , such that higher Reward Sensitivity was associated with an earlier onset of weekly alcohol use. According to MANOVA, hazardous and harmful drinkers (as defined by AUDIT) had significantly higher total FrSBe, Disinhibition, Executive Dysfunction, and Reward Sensitivity scores compared to low risk drinkers, Pillai's Trace  $F(6, 104) = 3.08$ ,  $p = .004$ , power = .90 (& AUDIT group comparisons significant by Tukey post-test,  $p < .05$ ).

**Conclusions:** Findings indicate that in a university sample of young adults, associations are present between indices of "frontal lobe" related traits and alcohol consumption levels. In such a young sample these associations likely reflect pre-alcohol traits that predispose to heavy drinking, as opposed to cumulative effects of high alcohol exposure - although the latter interpretation cannot be entirely ruled out.

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### NEUROCHEMICAL EFFECTS OF CITICOLINE TREATMENT IN METHAMPHETAMINE DEPENDENT PATIENTS: A LONGITUDINAL PROTON MAGNETIC RESONANCE SPECTROSCOPY STUDY.

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**Aims:** This study was aimed to assess the efficacy and safety of citicoline (cytidine-5'-diphosphate), a key intermediate for membrane phospholipids, in treating methamphetamine (MA) dependent patients. Secondary aim was to examine the effects of citicoline on neurometabolite levels using proton magnetic resonance spectroscopy (1H-MRS). We hypothesized that the cerebral level of n-acetylaspartate (NAA), a neuronal marker, would be increased with citicoline treatment via restoring the stability of neuronal membranes in MA dependent patients.

**Methods:** Thirty-one MA dependent patients were administered of citicoline (n=16) and placebo (n=15), respectively, for a 4-week of study period. Binary urine test results by week were analyzed as an outcome measure using generalized estimating equation modeling. Patients were also evaluated by 1H-MRS before drug administration, and 2 and 4 weeks following treatment.

**Results:** Significant group-by-week interaction effects favoring citicoline in maintaining MA abstinence were observed during a 4-week treatment period (week 1,  $p=0.002$ ; week 2,  $p=0.027$ ; week 3,  $p=0.018$ ; week 4,  $p=0.049$ ). A group-by-week interaction effect was found in prefrontal NAA levels (week 2,  $p=0.017$ ; week 4,  $p=0.028$ ), with citicoline treated group showing increases at 2- and 4-week time points, whereas placebo-controlled group had no change in prefrontal NAA levels over time.

**Conclusions:** These preliminary findings suggest that citicoline treatment has potential efficacy in maintaining abstinence relative to placebo. Additionally, citicoline treatment was associated with increases in prefrontal NAA levels in MA dependent patients.

**Support:** This study was supported by NIDA Bioengineering Grant (BRP, DA014178), DA015116 (P.F.R.) and NIDA DA024070 (P.F.R., I.K.L.). citicoline and placebo were supplied by the Ferrer.

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### ALTERATIONS IN MICROSTRUCTURE OF THE ISTHMUS IN MIDSAGITTAL CORPUS CALLOSUM IS ASSOCIATED WITH DURATION OF COCAINE USE IN THE COCAINE-DEPENDENT SUBJECTS.

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**Aims:** The corpus callosum (CC) is the largest white matter fiber network interconnecting the cerebral hemispheres in the human brain. Recent studies have demonstrated that diffusion tensor imaging (DTI) is capable of providing information regarding white matter integrity of the CC. In this study, DTI parameters were compared in cocaine dependent subjects (CDs) and non-drug using controls (NCs) in midsagittal CC.

**Methods:** DTI images were acquired from 19 CDs and 18 age-matched NCs on a Philips 3.0 T scanner. The midsagittal CC was segmented into 6 subdivisions: genu, rostral body, anterior midbody, posterior midbody, isthmus, and splenium. The mean values of the DTI metrics in each of the 6 CC segments were computed. Group comparisons on DTI metrics of the 6 CC segments were performed using SPSS Linear Mixed Models.

**Results:** Relative to the NCs, CDs had lower fractional anisotropy (FA), higher radial diffusivity ( $\lambda_{\perp}$ ), and higher mean diffusivity ( $\lambda_{\text{avg}}$ ) in the isthmus; higher  $\lambda_{\perp}$  and higher  $\lambda_{\text{avg}}$  in the rostral body; and lower FA in the splenium. In the isthmus of CDs, there was a significant negative correlation between FA and duration of cocaine use (DoCU), and a significant positive correlation between  $\lambda_{\perp}$  and DoCU.

**Conclusions:** The white matter integrity in the midsagittal CC was compromised in the CDs. The alterations in the rostral body are consistent with our previous findings in an entirely different group of CDs using a 1.5 T GE scanner. The alterations in the isthmus are likely to be associated with long-term cocaine use. The isthmus contains transcallosal fibers from the parietal, temporal, and sensorimotor areas, therefore the alterations in the isthmus may affect the normal function of these regions.

**Support:** This study was funded by National Institute on Drug Abuse Grants #P50 DA009262 and K02 DA00403 (FGM), and NIH-NINDS R01 NS052505-03 (KMH).

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**SUBSTANCE DEPENDENCE CRITERIA (DSM-IV) IN DAILY CANNABIS USERS.**

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**Aims:** To study the DSM-IV criteria for substance dependence among daily cannabis users.**Methods:** A qualitative method and an intentional sample of daily cannabis users in the community were adopted in this investigation, which was conducted in Sao Paulo, Brazil. In-depth, semi-structured interviews based on the DSM-IV criteria for substance dependence were held individually. The interviews were recorded and transcribed for posterior content analyses.**Results:** 24 people (15 men) aged 18-49 years participated in this study. Only one participant reported compulsive use, while the others planned cannabis use through their daily routine without reducing the frequency in which engaged in important activities. Impairments on the short-term memory were reported by 17 participants. There was no report of tolerance towards the sensation of relaxation, which was claimed to be the main motivation for continued use. Despite the fact only four participants were diagnosed dependent (DSM-IV), 16 considered themselves dependent.**Conclusions:** The specificities regarding tolerance and control/compulsion seem to reduce the probability of establishing diagnoses of dependence. There is a need for more thorough studies evaluating the specificities of the nature of the dependence claimed by this profile of users, and, perhaps, more specific criteria addressing the above-mentioned aspects regarding long-term daily cannabis users.**Support:** FAPESP and AFIP

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**THE POWER OF ELICITING CONSUMER INPUT TO DESIGN EFFECTIVE TREATMENT SYSTEMS.**Lynn Madden<sup>1</sup>, A Quanbeck<sup>2</sup>, S O Farnum<sup>2</sup>, J H Ford<sup>2</sup>, S Ball<sup>1</sup>; <sup>1</sup>APT Foundation and Yale University, New Haven, CT, <sup>2</sup>University of Wisconsin, Madison, WI**Aims:** To show that by systematically eliciting and analyzing the preferences of consumers an agency can create a more accessible, more effective treatment system that encourages improved efficiencies and financial performance. A customer driven model is the foundation of classic economic theory and the key to product improvement. Agency management strategies drawn from the business world are valid not for a profit motive per se; but rather in that all successful business models are customer driven.**Methods:** Principles critical to improving performance of substance abuse treatment services are (1) offering services that consumers can and will use (2) services that can be paid for, and (3) services that improve consumer outcomes. It is important to use transparent metrics understandable to payers, clinical staff and clients to evaluate service offerings and improvements.**Results:** The primary focus of performance improvement to date has been to effectively serve current demand. In the short run, demand is considered fixed; the NIATx aims of achieving improved access and retention are the first steps in improving both clinical and financial performance. Methods proven to increase access are informed by identifying and eliminating barriers. Retention is improved by shifting programs to be more reinforcing; both aims are achieved by making changes based on consumer feedback.

Agencies that operate efficiently, as defined by consumers, create strategic advantage, ie; the ability to attract payers and clients and the opportunity to shift the supply curve, rather than the just the more traditional efficient servicing of current demand. Gap analysis is also a strategy for shifting the supply curve; identifying market needs and providing services to satisfy unmet demand.

**Conclusions:** Systematically using client feedback, especially that related to access and retention, is a method of moving an agency to improved client outcomes, efficiencies and business performance.**Support:** Support: National Institute on Drug Abuse (5 R01 DA020832-02) and Robert Wood Johnson Foundation (59714)

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**PREDICTING RECENT EVENT-LEVEL CONDOM USE USING BEHAVIORAL ASSESSMENT AMONG URBAN, MINORITY SUBSTANCE USERS.**

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**Aims:** Risky sexual behavior (RSB) is a leading cause of HIV, particularly among urban drug users that face heightened HIV risk due to high rates of exchange of sex for drugs/money and IV drug use. The examination of specific predictors of RSB is of great relevance to understanding HIV risk; however, previous studies have mainly utilized global measures of risky sexual behavior that are limited by inaccuracy of recall, particularly in substance using samples.**Methods:** To enhance accuracy of RSB assessment, an event-level approach may be useful. Additionally, behavioral assessments of relevant constructs may be less transparent than self-report measures. The Balloon Analogue Risk Task (BART) is a computerized, behavioral measure of risk taking propensity that uses contingencies to measure actual "risk taking" in the laboratory. The goal of the current study was to incorporate a multi-dimensional, multi-modal assessment of personality and environmental predictors of RSB in an illicit drug using sample, measuring RSB using event-level data of condom use at one's most recent sexual encounter.**Results:** Using a sample of 156 illicit drug users residing at a Washington, DC drug treatment center (M age = 41.85; SD = 8.59; 75% male), we conducted a multivariate logistic regression analysis predicting condom non-use at one's last sexual encounter, examining the incremental validity of the BART after accounting for the key variables related to one's engagement in RSB (age, partner type, drug use frequency, and attitudes towards condoms). Entered in the final step, the BART was a significant predictor above and beyond these other variables (step  $\chi^2 = 6.80$ ,  $p = .009$ ).**Conclusions:** These findings demonstrate the utility of behavioral assessment of risk-taking propensity to predict condom non-use at one's most recent sexual encounter and suggest this type of objective measurement may serve as a useful complement to more traditional risk factors in efforts to better understand, prevent, and intervene with RSB among inner-city drug users.**Support:** NIDA R01DA019405

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**VALIDATING SELF-REPORTS OF ILLEGAL DRUG USE TO EVALUATE NATIONAL DRUG CONTROL POLICY.**

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**Aims:** The Office of National Drug Control Policy evaluates the effectiveness of national drug demand reduction policies by highlighting measures of change in drug use from several annual/biennial national surveys. This paper conducts secondary analysis of a major validity study of self-reported drug use in the National Survey of Drug Use and Health (NSDUH) to determine whether that study's largely favorable conclusions are justified (Harrison et al., 2007).**Methods:** The validity study compared past 30-day self-reported drug use to urinalysis for a sample of 12-25 year-olds in the NSDUH. Respondents were asked to provide urines after their self-reports were obtained. Published data tables were re-analyzed for marijuana and cocaine. (Methodological problems preclude analysis for other drugs.)**Results:** For marijuana, the 2 X 2 table is as follows: self-report-no/urine-negative (n=3,117, 82.9% of total sample); self-report-no/urine positive (n=165, 4.4%) self-report-yes/urine-negative (n=218, 5.8%); self-report-yes/urine-positive (n=259, 6.9%). The validity study estimated 30 day marijuana prevalence as 4.4% + 5.8% + 6.9% = 17.1%. However, this assumes that all 3,117 who denied use and tested negative reported accurately. Instead, we make the more plausible assumption that marijuana users who test negative deny use at the same rate as known users (i.e., those testing positive). (Urine may be negative when use is prior to the reliable 3-7 window of detection.) Do this backcalculation: 165/259 = .637; .637 = 139 = 3.7% of the sample. Imputing these additional users suggests 20.8% marijuana prevalence. Similarly, the validity study estimated cocaine prevalence as 2.0%, whereas the imputation technique suggests 4.2% prevalence.**Conclusions:** Using a plausible imputation technique, true national prevalences may be 1.64 & 4.67 times as high for marijuana & cocaine, respectively, than estimated by self-reports alone. Small differences over time in the willingness of youths to reveal drug use, e.g., because of increased stigmatization of use prompted by anti-drug campaigns, can be mistaken for decreases in use.**Support:** Evaluation Center, WMU

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### **SOUTH ASIAN WOMEN AND DOMESTIC VIOLENCE: ISOLATION, SOCIAL SUPPORT, HELP-SEEKING, AND ADDRESSING RISKS OF CO-OCCURRENCE OF SUBSTANCE ABUSE AMONG INTIMATE PARTNERS.**

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**Aims:** This study aimed to document the extent of domestic violence among a community sample of South Asian women in the United States, and to investigate socio-cultural factors associated with domestic violence in this population. It also assessed the extent of help-seeking among the sample who are victims of domestic violence.

**Methods:** Both paper and Web-based questionnaires were used to conduct a cross-sectional survey of South Asian women residing in the United States of America. Convenience and snowball sampling procedures were used and 215 cases were included in the multivariate logistic regression analyses.

**Results:** Results indicated that 38% of women of South Asian origin experienced psychological abuse, physical abuse, sexual abuse, and/or injury from abuse in the past year. Psychological abuse was by far the most prevalent form of abuse (52%), and as many as 48% of the women who were abused experienced physical abuse, sexual abuse, or injury. Isolation, as measured by ties with spouse/partner, and perceived social support were predictors of both abuse and help-seeking. Isolation, as measured by ties with family, friends, and social and cultural groups, was also a predictor of help-seeking.

**Conclusions:** Among the study's practice and policy implications for preventing domestic violence is a need to reach out to South Asian women in the community to ensure that they are not isolated and concentrate on increased risk and early onset of substance abuse problems that is strongly related with domestic violence. The information will contribute to designing culturally appropriate interventions to recognize comorbidity of domestic violence and substance abuse and prevent domestic violence in this group.

**Support:** -Harry E. & Bernice M. Moore Fellowship, Hogg Foundation for Mental Health, The University of Texas at Austin(2008-2009)

-The Tarakanth Das Foundation Scholarship, Southern Asian Institute at the School of International and Public Affairs, Columbia University, New York(2007-2008)

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### **PERSISTENCE OF CANNABIS USE ONCE IT STARTS: INITIAL FINDINGS FROM EPIDEMIOLOGICAL RESEARCH.**

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**Aims:** In a small but noteworthy fraction of cannabis smokers, a cannabis dependence syndrome develops within 1-2 years after onset of first cannabis use in a process that starts with an increasing number of days of cannabis use that drives, and is driven by, a drug dependence process. It seems that this process engages male cannabis smokers more than females and early adolescent smokers more than later-onset smokers. In this large-sample epidemiological research, we seek a more complete understanding of population sub-group variation in persistence of this cannabis process, with a focus on male-female and race-ethnicity variation in the experience of recent-onset cannabis smokers (ROCS), defined to include individuals who started cannabis smoking within 24 months of field survey assessment.

**Methods:** Data are from 1,968 ROCS self-identified among the 55,279 National Survey on Drug Use and Health(NSDUH)participants who completed confidential computer-assisted self-interviews in 2006. Analyses of sub-group variation are based upon a Poisson count regression model for the frequency of cannabis smoking in the month just prior to the date of assessment, with due attention to NSDUH sample design and weights.

**Results:** Among all participants, 33,780 had smoked cannabis at least once, but only 1,968 qualified as ROCS. The vast majority (66%) of ROCS were 12-17 years old who tended to have progressed to more frequent cannabis smoking than their older counterparts (e.g., those starting cannabis use after age 20;  $p < 0.05$ ). Independently, male ROCS had more frequent cannabis smoking days than females ( $p < 0.05$ ). As compared to non-Hispanic White ROCS, Asian and Pacific Island ROCS had less frequent cannabis smoking days ( $p < 0.05$ ).

**Conclusions:** This new evidence supports the idea that males and adolescent-onset users are more likely to persist in cannabis smoking beyond the first 1-2 occasions of use. Extension of this research will include a focus upon a very rapidly developing cannabis dependence process within the first quarter of the year after onset of cannabis smoking.

**Support:** NIDA awards K05DA015799 & T32DA021129.

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### **UTILITY OF VARIOUS SCREENING INSTRUMENTS FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN RESEARCH PARTICIPANTS SEEKING TREATMENT FOR COCAINE DEPENDENCE.**

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**Aims:** To date, there are scant data assessing the clinical utility of commonly used ADHD screening instruments in substance-abusing populations. The purpose of this study was to assess the sensitivity, specificity, positive and negative predictive values of commonly used screening instruments for attention-deficit hyperactivity disorder in cocaine-dependent individuals seeking treatment. Using the Conner's Adult ADHD Diagnostic Interview for DSM-IV (CAADID) we predicted that interrater reliability on the CAADID between trained research therapists would be high and that the ADHD Rating Scale (AARS), Wender Utah Rating Scale (WURS), and the Adult ADHD self-report scale (ASRS-v1.1) Part A would have clinical utility to screen individuals for the presence/absence of ADHD.

**Methods:** The AARS, WURS, ASRS, and CAADID instruments were completed; all participants were screened during 2008. The interrater reliability of the CAADID was determined using a kappa coefficient along with the sensitivity, specificity, positive and negative predictive values of each of the screening instruments using the CAADID as the gold standard.

**Results:** The sample consisted of 32 participants, 82 % male; 29% Caucasian, 39% Hispanic, 25% African American and 7% Other; 41 +/- 20 years. Interrater reliability was high (kappa = .89). Sensitivity was 1 for both the AARS and WURS, with specificity being .95 and .91 respectively. Although specificity for the ASRS was high (.82), its sensitivity was low (.4). PPV and NPV were high among the AARS and WURS (PPV = .83, .71; NPV = 1,1). However, the ASRS revealed low PPV (.33) and high NPV (.9).

**Conclusions:** The CAADID is a reliable instrument for diagnosing ADHD among cocaine abusers. All screening instruments had high specificity and negative predictive validity. The AARS and WURS are good screening tools for this dually diagnosed population. Although the ASRS appropriately screens individuals out for ADHD, its sensitivity and PPV is low.

**Support:** NIDA # R01DA23652, K23DA021209, K02DA00465

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### **ANTIDEPRESSANT-LIKE EFFECTS OF MDMA IN A ANIMAL MODEL OF DEPRESSION.**

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**Aims:** MDMA produces enhanced mood and other immediate effects in humans as a result of increased synaptic serotonin (5-HT) levels. This action may underlie antidepressant-like effects of MDMA that may be more prominent in subjects with mood disturbance. Flinders Sensitive Line (FSL) strain is the principal animal model of depression. These rats are more immobile in the Forced Swimming Test (FST), which is used to detect depressive-like states in animals. The intracellular concentrations of 5-HT and its main metabolite, 5-hydroxyindoleacetic acid (5-HIAA), are higher in FSL than in Sprague-Dawley (SD) rats possibly reflecting decreased extracellular 5-HT. The immobility of FSL rats is reversed by known antidepressants after prolonged administration. The aim of this study was to determine whether MDMA administration has a dose-dependent antidepressant-like effect in an animal model of depression.

**Methods:** 24 SD and 24 FSL male rats (8 weeks old) were divided into 3 treatment groups (n=8 of each strain): 0.9% saline, MDMA 5mg/kg and 10mg/kg. 2 FST sessions (5 min each) were carried out: 30 min after initial injections and after 3 weeks of treatment. Total immobility time was recorded. Cortical levels of 5-HT and 5-HIAA were determined using HPLC-ECD after 3 weeks of treatment.

**Results:** In the initial FST dose-dependent decreases in immobility time were observed in both strains; they were more pronounced in the FSL resulting in 'normalisation' of behaviour following the 10 mg/kg dose. FSL control and MDMA5 rats were more immobile than SD rats. After repeated administration the antidepressant-like effect of MDMA was still present, but much less pronounced. Intracellular levels of 5-HT and 5-HIAA were substantially higher in FSL than in SD rats in all treatment groups. MDMA administration for 3 weeks did not affect these levels in either strain.

**Conclusions:** Acute MDMA administration leads to a significant decrease in immobility in FSL rats and reverses their depressive-like state. The antidepressant-like effects of MDMA are diminished after repeated administration, possibly due to tolerance.

**Support:** This project was supported by a grant from the NHMRC.

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**CIRCUITS IN METHAMPHETAMINE CUE CRAVING AND CUE EXTINCTION.**

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**Aims:** The primary aims of this pilot project were to develop procedures to assess brain imaging circuitry of visual cue-generated craving and cue extinction in non-treatment seeking methamphetamine subjects.

**Methods:** We used serial fMRIs to elucidate neural circuitry activated by visual cues and altered by cue extinction. Subjects were 9 male and 1 female Caucasians with a mean age of 34, and mean years of methamphetamine use of 9.5. Three fMRIs scans were performed in a Phillips 3.0 T over an eight day interval. The first scan was for cue activation, the second two scans occurred under conditions of cue extinction (no meth exposure with repeated visual cues). Ten healthy controls completed a single identical cue activation scan. We used a 12-minute sequence for visual stimulus presentation. A block design was used presenting visual control pictures, meth use pictures, and visual rest conditions. Subjective cravings for methamphetamine were measured in real time at the end of each block of methamphetamine-neutral and visual rest conditions.

**Results:** Using a meth minus neutral subtraction, scan one revealed activation of the medial prefrontal cortex, parahippocampal cortex, left head of the caudate nucleus, superior parietal cortex, and bilateral inferior temporal cortex. The second scan showed activity in parietal and temporal cortex. Parietal and inferior temporal cortex remained active (minimum voxel size 15,  $p < 0.001$  for all regions of interest). Subjective craving for meth was rated low in all scans.

**Conclusions:** Despite low craving scores and two extinction trials, parietal and temporal cortex activity remained robust, possibly indicating that extinction learning was an ongoing dynamic process.

**Support:** NIH/NIDA

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**INTER-RATER RELIABILITY AND VALIDITY OF DSM-IV OPIOID DEPENDENCE IN A HMONG ISOLATE USING THE SEMI-STRUCTURED ASSESSMENT FOR DRUG DEPENDENCE AND ALCOHOLISM THAI VERSION.**

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**Aims:** The use of isolated populations is an important strategy to map genes for complex traits due to relative genetic and environmental homogeneity. However, reliable and valid phenotypic characterization of the disease in the study population is essential. We examined diagnostic reliability and concurrent validity of DSM-IV opioid dependence (OD) in a Hmong village in Thailand with historically high rates of opium/heroin use.

**Methods:** 123 Thai-speaking Hmong individuals were assessed for lifetime OD, using Thai versions of the Semi-Structured Assessment for Drug Dependence and Alcoholism (SSADDA-Thai) and Mini-Neuropsychiatric Interview (MINI-Thai; adapted for lifetime diagnoses). Two raters interviewed each subject independently within a 2-week period. Chance-corrected agreement on OD diagnosis was assessed between raters and instruments.

**Results:** Results showed excellent agreement both within (SSADDA-Thai:  $\kappa = 0.97$ ; MINI-Thai:  $\kappa = 0.95$ ) and between ( $\kappa = 0.98$ ) instruments with respect to a DSM-IV diagnosis of OD.

**Conclusions:** Consistent with reliability assessments of English versions, our data demonstrate high reliability for Thai versions of the SSADDA and MINI with respect to OD. The high concordance between instruments supports the concurrent validity of the diagnosis. Either interview appears to provide reliable, valid OD diagnoses in Thai-speaking Hmong individuals.

**Support:** Supported by NIH grants K24DA017899, R01DA018363, D43TW006166, and R01DA12690

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**COMPARING JURISDICTIONAL POLICIES TO BUPRENORPHINE-NALOXONE IN AUSTRALIA.**

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**Aims:** Daily supervised medication administration is a defining characteristic of opioid maintenance treatment in Australia. Buprenorphine-naloxone (BNX) was formulated to reduce the abuse liability of buprenorphine, potentially allowing greater scope for unsupervised administration. Each of the 3 Australian jurisdictions studied have adopted a different policy for BNX, varying on aspects such as who can prescribe the medication, the number of unsupervised doses, and which patient variable indicate suitability for takeaways. We investigated the impact of these jurisdictional differences on compliance with policy, client outcomes, and doctor and client experiences of BNX treatment.

**Methods:** A mixed quantitative and qualitative design was used. Sixty-one doctors and eighty-five patients from three Australian states participated. Data collection consisted of questionnaires, medical record audits and focus groups. Prescribing compliance and treatment outcome data was analysed using parametric and non-parametric statistical tests. A thematic analysis of qualitative data was conducted. Data triangulation was used to enhance validity.

**Results:** State differences were found in doctors' compliance with policy and doctors' and patients' experiences of treatment. There were, however, few differences in treatment outcomes. Patients in the state with the most restrictive policy expressed frustration with treatment and were more likely to want to cease maintenance treatment. In the state where highly selected patients had greater access to unsupervised medication, doctors' compliance with guidelines was best and patients felt their treatment progress had been recognised. In the state with the most flexible policy, doctors' compliance with policy was lowest and patients and doctors wanted more support.

**Conclusions:** The implications for future decisions about BNX policy in Australia will be presented and the importance of contextual factors in formulating drug policy examined.

**Support:** Australian Ministerial Council on Drug Strategy

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**FACTORS ASSOCIATED WITH NEEDLE EXCHANGE PROGRAM AND PHARMACY USE AMONG HEROIN AND COCAINE INJECTORS IN BALTIMORE, MD.**

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**Aims:** Many studies examining the use of needle exchange programs (NEPs) by injection drug users (IDUs) are limited because they do not consider other verifiably safe sources of needle acquisition, such as pharmacies. This study examined the factors associated with obtaining most new needles/syringes from a pharmacy, a NEP, or some other source among IDUs in Baltimore, MD.

**Methods:** Adult heroin and cocaine injectors (304) were recruited from the community into an epidemiologic study of risk factors for HIV/AIDS. Multinomial logistic regression was used to examine the association between where IDUs obtained most of their new needles and several independent variables that were shown to be associated in extant literature.

**Results:** Findings showed that those using pharmacies (vs. another source) were more likely to be male (COR=3.07, 95% CI=1.60-5.89), white (COR=6.36, 95% CI=2.31-17.50), and have at least a high school diploma (COR=2.61, 95% CI=1.35-5.03), and less likely to share injection equipment (COR=0.48, 95% CI=0.25-0.93). Also, those using NEPs (vs. another source) were more likely to inject more frequently (1-2 times/day vs. <1 time/day, COR=3.48, 95% CI=1.36-8.93; 3 times/day vs. <1 time/day, COR=4.82, 95% CI=2.08-11.21), and to have been arrested for drug paraphernalia (COR=4.65, 95% CI=1.31-16.55) and less likely to live farther away from a NEP (COR=0.34, 95% CI=0.12-0.92), to share injection equipment (COR=0.48, 95% CI=0.23-0.99), and to reuse needles (COR=3.31, 95% CI=1.34-8.20).

**Conclusions:** The findings suggest that NEPs and pharmacies may serve different populations of IDUs and may play complementary roles in the prevention of infectious diseases such as HIV/AIDS and Hepatitis.

**Support:** This research was supported by NIDA RO1 Grant DA014498 and NIDA T32 Grant DA007292.

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### A RANDOMIZED PLACEBO CONTROLLED TRIAL OF SERTRALINE AND SERTRALINE PLUS GABAPENTIN IN DEPRESSED, RECENTLY ABSTINENT COCAINE-DEPENDENT PATIENTS.

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**Aims:** To Determine if treatment with sertraline or sertraline plus gabapentin improved treatment retention, depressive symptoms and/or cocaine use.

**Methods:** Depressed cocaine dependent patients (N=87) were enrolled in this 12-wk, double blind, randomized, placebo-controlled, clinical trial and placed in research beds at a residential treatment facility (RCA). They were randomized by depressive symptom severity to receive one of the following: sertraline alone (200 mg/day), sertraline (200 mg/day) plus gabapentin (1200 mg/day), or placebo. Subjects were inducted onto the maintenance dose of study medication (weeks 1-2) while residing in RCA. Participants transferred to outpatient treatment at the start of their third week, continued receiving study medications or placebo (wks 3-12) and participated in weekly individual CBT. Compliance with study requirements was facilitated through the use of contingency management procedures. Supervised urines were obtained thrice weekly; self-reported mood was obtained weekly. At the end of 12 weeks, participants were tapered off the study medication over a 5 day period and referred to a local treatment program, if interested.

**Results:** 105 participants will be enrolled, but to date 87 have been entered. Thus far, results show that subject characteristics and retention did not differ among the groups. Hamilton depression ratings significantly decreased over time regardless of treatment group ( $p < 0.0001$ ). The proportion of cocaine-positive urines was significantly less in the sertraline ( $p = 0.03$ ), but not sertraline-gabapentin group ( $p = 0.50$ ), relative to the placebo group. The sertraline group (39.2 days,  $p = 0.06$ ), but not sertraline-gabapentin group (31.2 days,  $p = 0.26$ ), showed a trend toward a greater mean time to the first cocaine-positive urine relative to placebo (20.9 days).

**Conclusions:** These preliminary results suggest that sertraline alone facilitates relapse prevention in depressed, recently abstinent cocaine dependent patients.

**Support:** NIDA grant P50 DA12762 and Arkansas Biosciences Institute

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### HIV RISK BEHAVIORS BY SEXUAL ORIENTATION AFTER TREATMENT FOR METHAMPHETAMINE DEPENDENCE.

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**Aims:** To examine HIV risk behaviors by self-reported sexual orientation.

**Methods:** A recently completed longitudinal follow-up of the Methamphetamine Treatment Project (MTP), an 8-site study of treatment for methamphetamine dependence, interviewed 587 MTP participants approximately 3 years after treatment intake to collect information across a range of domains. Of those who provided information on sexual orientation (heterosexual = 543; gay/lesbian = 17; bisexual = 24), data was analyzed addressing high-risk injection drug use and sexual behaviors collected with the TCU HIV/AIDS Risk Assessment.

**Results:** Results document similar rates of participants in each group who reported injecting drugs in the last 6 months (11.4%, 11.8%, 16.7% for heterosexual, gay/lesbian, and bisexual groups, respectively). Among those who reported injecting drugs in the last 6 months, a larger percentage of those in the gay/lesbian and bisexual groups reported doing so at least 1 time/week (gay = 11.8%; bisexual = 12.5%), as compared to 6.5% of the heterosexual group. The percentage of those in each group who reported having sex without using a latex condom/barrier with someone not their spouse or primary partner was 18.1% for the heterosexual group, 26.7% for the gay group, and 9.1% for the bisexual group.

**Conclusions:** Additional findings will be presented addressing other high risk behaviors, as well as high risk behaviors by sexual orientation and current methamphetamine use.

**Support:** Data collection for this study was funded by CSAT, contract #270-01-7089.

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### CHARACTERISTICS OF CLIENTS WITH CO-OCCURRING DISORDERS IN ADDICTION TREATMENT: A COMPARISON BY GENDER.

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**Aims:** The study examines gender differences in clients with co-occurring psychiatric and substance use disorders (COD) receiving addiction treatment.

**Methods:** Males ( $n = 450$ ) and females ( $n = 774$ ) were compared on demographic, social, psychiatric, substance use, and treatment characteristics.

**Results:** On demographic and social variables, females were more likely to be Black, younger, living in an institutional setting, and legally involved, whereas males were more often Hispanic and homeless. In the psychiatric domain, females were more often diagnosed with posttraumatic stress disorder and males more frequently obtained diagnoses of depression and generalized anxiety disorder. Males reported greater symptom severity on the Brief Symptom Inventory and received higher severity ratings by clinicians on the Brief Derogatis Psychiatric Rating Scale. Examination of substance use patterns revealed that males were more likely to use alcohol and opiates as their primary substances, whereas females more often used crack cocaine and methamphetamines. Further, a higher percentage of females reported polysubstance use. Females also reported more psychosocial problem days; by contrast, men reported more problem days due to substance use. At discharge, males had higher rates of treatment completion and past month abstinence and AA attendance. Females were more likely to have left treatment against medical advice.

**Conclusions:** Results indicate that in this sample of COD clients, males displayed greater psychiatric symptom severity but reported less psychosocial problem days at admission to treatment. Conversely, females reported higher levels of psychosocial distress and less problem days related to substance use compared to men. These findings suggest that males may be more willing to admit to problems related to substance use and females more open to acknowledging the effects of psychological problems. Results indicate that clients of both genders may benefit from programming focusing on the interaction between psychiatric and substance use issues.

**Support:** Texas Co-Occurring State Incentive Grant, SAMSHA.

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### PATTERNS OF BUPRENORPHINE DOSE REDUCTION IN OPIOID-DEPENDENT PATIENTS.

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**Aims:** Buprenorphine (BUP) was approved by the FDA for office-based treatment of opioid dependence in October 2002. To date, there is limited research on tapering schedules of BUP after long-term treatment. With the increasing prevalence of prescription opioid use (SAMSHA 2007), and the greater numbers of people receiving BUP, it is important to understand how people terminate this medication. A chart review to investigate patterns of BUP dose reduction was performed on a subset of 16 patients from the Columbia University Buprenorphine Program. Dose reduction was based on patients' subjective experience: patients reduced BUP doses based on convenience and ability to tolerate withdrawal symptoms.

**Conclusions:** Patients were primarily male (88%) and white (81%) with an average age of 42. Thirty-one percent reported having chronic pain; of these, 6% were receiving another type of pain treatment (i.e. epidural). Average length of time in the program was 2.2 years. Average maintenance dose after 2 weeks on buprenorphine was 21 mg (8-32 mg). The average post-taper dose was 5.3 mg (0-16 mg). The mean length of time it took to decrease from 32 to 24 mg was 13 months. Other times for dose reductions follow: from 24 to 16 mg = 6.4 months, 16 to 8 mg = 12.8 months, 8 to 4 mg = 8.7 months, 4 to 2 mg = 4.3 months, and 2 to 0 mg = 9.3 months. The most common side effect reported from patients tapering from 32 to 8 mg was insomnia (31%), and from 4 to 1 mg were muscle aches (25%) and anxiety (25%). One patient requested adjuvant medications (i.e., clonazepam, clonidine) to treat withdrawal symptoms. Concomitant medication use during the taper was anti-anxiety medications (including benzodiazepines, 38%), anti-depressants (25%), and insomnia medications (38%). Only one difference emerged when comparing pain patients to substance abuse patients, namely, it took pain patients longer to taper from 24 to 16 mg (mean 12 vs. 2 months,  $p < .02$ ). More research is needed to help guide clinicians taper patients from buprenorphine after long-term treatment.

**Support:** None

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### ACTIVATION OF MGLUR2/3 SELECTIVELY ATTENUATES COCAINE CUE-MEDIATED BEHAVIOR IN A NOVEL NONHUMAN PRIMATE MODEL OF RELAPSE.

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**Aims:** Activation of group II metabotropic glutamate receptors (mGluRs) can attenuate cue-induced reinstatement of cocaine-maintained behavior. However, these procedures typically impose an extinction condition which is uncommon in humans. We therefore sought to examine the effects of group II mGluR activation in a novel nonhuman primate model of cue-induced cocaine-seeking behavior.

**Methods:** Squirrel monkeys (n=4) were trained on a mixed S+/S- second-order schedule of i.v. cocaine self-administration. Responding during S+ sessions was reinforced by i.v. infusions of cocaine under a fixed-interval 600-sec with fixed-ratio 20 response components. During S- sessions, cocaine and cocaine-associated cues were absent. To investigate the impact of group II mGluR activation on cocaine cue-induced behavior, subjects were pretreated with the mGluR2/3 agonist LY379268 (0.1–1.0mg/kg, i.m.) 30-min prior to the start of a S+ session. Selectivity of pretreatment effects were determined in a separate group of squirrel monkeys (n=3) trained under an identical schedule of stimulus-avoidance.

**Results:** All subjects emitted high rates of responding during S+ sessions, whereas response rates were significantly lower during S- sessions. Self-administration animals emitted high rates of responding during the first component when behavior was maintained solely by cocaine-associated stimuli. LY379268 dose-dependently decreased cocaine cue-induced operant behavior during S+ sessions, an effect which was apparent during the first, drug-free component. In contrast, none of the doses tested affected operant behavior in animals trained under an identical schedule of stimulus-avoidance.

**Conclusions:** These findings demonstrate that pharmacological activation of group II mGluRs selectively attenuates cocaine cue-mediated behavior in squirrel monkeys. Furthermore, we propose the mixed S+/S- second-order schedule as an effective model of cue-induced drug relapse in nonhuman primates.

**Support:** This work supported by USPHS grants DA12514, DA00517, T32 DA015040, T32 GM08605-11, and RR00165.

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### EFFECTS OF METHAMPHETAMINE AND MDMA ON SPEECH.

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**Aims:** The effects of methamphetamine (MA) and MDMA (Ecstasy) on speech have not been evaluated under controlled conditions. The present study used a within-participant design to compare the effects of MA and MDMA on multiple measures of spontaneous speech.

**Methods:** Eleven recreational amphetamine users completed this double-blind, 13-day residential laboratory study, which consisted of 4 three-day blocks of sessions. On the first day of each block, participants received placebo, MA (20, 40 mg) or MDMA (100 mg); the remaining two days of each block were drug "washout" periods. Ninety minutes after drug administration, participants summarized films they viewed the previous evening and then completed visual analog scales. Descriptions were recorded and coded for quantity of speech and fluency. In addition, to determine if MA- and MDMA- related effects were apparent perceptually, 40 undergraduates listened to the film descriptions and rated them for coherence and mood of the talkers.

**Results:** MA increased quantity of speech, verbal fluency, and subjective ratings of "talkative" and "alert." By contrast, MDMA increased average lengths of filled pauses (e.g. "um," "er") and subjective ratings of "can't concentrate." Both drugs decreased average lengths of nonjuncture unfilled pauses. Listener-rated descriptions indicated that MA significantly increased the focus and coherence of the talkers.

**Conclusions:** In general, the data indicate that MA improved speech fluency, while MDMA produced some disruptions in fluency. These findings suggest that some general cognitive effects produced by MA and MDMA are manifest in distinctive measures of verbal fluency and perceived by naïve listeners.

**Support:** This research was funded by a grant from NIDA (R01 DA03746).

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### NALTREXONE-INDUCED PROTRACTED OPIOID WITHDRAWAL.

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**Aims:** Naltrexone, an opioid receptor antagonist, has achieved limited acceptance as a treatment for opioid dependence. It remains unclear if naltrexone influences withdrawal symptoms beyond that related to opioid discontinuation. We hypothesized that opioid withdrawal measures would be greater in individuals who received higher doses of naltrexone during treatment initiation.

**Methods:** Using two dosing strategies of naltrexone, we compared the severity of opioid withdrawal symptoms in 87 opioid-dependent patients. After inpatient detoxification, patients received 50 mg of oral naltrexone and were randomized under double-blind conditions to receive an injection of either 384 mg of naltrexone or placebo. All patients were maintained on oral naltrexone 50 mg daily for 24 weeks.

**Results:** Patients who received the naltrexone injection had significantly higher Subjective Opiate Withdrawal Scale (SOWS) scores than those who received placebo [33.6(±14.0) vs. 27.4(±7.0); t=2.2; p=0.03], one week after receiving the injection. Mean SOWS scores decreased significantly from baseline to one week post-injection among the placebo group [34.6(±15.1) vs. 27.5(±7.2); t=2.3; df=20; p=0.03], but not among the active medication group [33.4(±11.9) vs. 33.5(±13.6); t=-0.04; df=31; p=0.97]. One week post-injection, the mean serum levels of naltrexone and 6-β-naltrexol were significantly higher in the naltrexone injection group as compared to placebo; [naltrexone=5.0 ng/ml(±4.0) vs. 0.5 ng/ml(±1.4); t=4.6; df=26; p<0.001][6-β-naltrexol: 20.9 ng/ml(±4.0) vs. 6.1 ng/ml(±4.0); t=3.0; df=20.2; p=0.01].

**Conclusions:** Among patients receiving orally-administered naltrexone, those who received an additional intramuscular injection of 384 mg of naltrexone reported more severe opioid withdrawal symptoms than those who received placebo. These results suggest that depot naltrexone following detoxification prolongs opioid withdrawal symptoms. Future research should evaluate potential adjunctive treatments to enhance naltrexone tolerability.

**Support:** R01 DA10746, K23 DA021209, K23 DA021850, K02 DA00465, K24 DA022412

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### PREDICTORS OF OUTCOME IN BUPRENORPHINE TREATMENT FOR OPIOID-DEPENDENT YOUTH.

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**Aims:** This study examined predictors of treatment outcome among opioid-dependent youth in a randomized, clinical trial comparing the efficacy of various dosing regimens (28 vs. 63-day detoxification) of buprenorphine when combined with behavioral treatment.

**Methods:** Opioid-dependent youth (n = 41; aged 13-24 years eligible) were provided with behavioral treatment for 63 days, along with a double-blind buprenorphine taper for either 28 or 63 of their treatment days. Multiple regression analyses were conducted to examine the unique contributions of various predictors (baseline participant characteristics and psychiatric diagnostic status) to each outcome measure (treatment retention and weekly opioid abstinence as measured via urine toxicology), after considering treatment condition.

**Results:** Three variables accounted for a significant proportion of variance (34.9%) in the number of days participants were retained in treatment. Being referred from a needle exchange program to the treatment program and having a diagnosis of manic episode disorder were associated with poorer retention, while a diagnosis of conduct disorder was associated with greater retention. Three variables accounted for a significant proportion of variance (37.4%) in the number of weeks participants were documented to be opioid abstinent. Having a diagnosis of manic episode disorder was associated with less opioid abstinence, while having a diagnosis of conduct disorder or mixed anxiety depressive disorder was associated with greater opioid abstinence.

**Conclusions:** To our knowledge, this study represents the first systematic examination of an array of predictors of treatment outcome for opioid-dependent youth receiving combined behavioral-buprenorphine treatment. Results identified several clinically important relations between participant baseline characteristics and treatment outcome, which suggest the need for ancillary services for various sub-populations of opioid-dependent youth.

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**COHORT DIFFERENCES IN NONMEDICAL PRESCRIPTION DRUG USE IN ADOLESCENCE.**

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**Aims:** It is not known whether increases in adolescent nonmedical use of prescription drugs (NMPD) translated into increases in the public health burden and whether characteristics of adolescent NMPD users have changed over time. This study aims to test for cohort effects across time in NMPD use among adolescents aged 12-14 and 15-17 from 1999 to 2006 (e.g., adolescents aged 12-14 years old in 1999 will be 15-17 years old in 2002).

**Methods:** Secondary analysis of adolescent data (12-17 year-olds) from the National Survey of Drug Use and Health (NSDUH) years 1999 (n=18,685) to 2006 (n=18,314). Data was analyzed through basic contingency tables, proportion and 95% CIs, and weighted logistic regression models adjusted for sex and race/ethnicity. Significance of between-survey differences in prevalence estimates were assessed using two-sample Z-tests.

**Results:** Past-year NMPD use was defined as any NMPD use of opioids, stimulants, sedatives and tranquilizers. In 1999, 4.9% of respondents that were 12-14 year old were past-year NMPD users. In 2002, 13.5% of those that were 15-17 years old (same age cohort) were NMPD users (a 176% increase). Similar patterns of cohort increases in NMPD use were found when comparing cohort data from other years (e.g., comparing 2003 vs. 2006 data there was a 111% intra-cohort increase in NMPD use). Past-year NMPD use increases across time were higher among females than males (2002 vs. 1999: aOR=1.2[1.0-1.4]; 2006 vs. 2003: aOR=1.2 [1.1-1.4]) and among Whites versus African-Americans (2002 vs. 1999: aOR=1.6[1.2-1.9]; 2006 vs. 2003: aOR=1.4[1.1-1.7]). There was a trend for increases to be higher among Hispanics versus African-Americans across time.

**Conclusions:** Past-year NMPD use greatly increased among adolescent birth cohorts as they aged in the past few years, possible factors that lead to this increases need to be further investigated.

**Support:** Funding source: NIDA grant DA023434 (P.I. Martins).

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**THE ROSTRAL BASOLATERAL AMYGDALA AND PRELIMBIC PREFRONTAL CORTEX ARE SERIALY CONNECTED TO REGULATE REINSTATEMENT OF COCAINE-SEEKING BEHAVIOR IN RATS.**

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**Aims:** Recent research posits a role for both the rostral basolateral amygdala (rBLA) and prelimbic prefrontal cortex (plPFC) in regulating cue-induced reinstatement of cocaine-seeking behavior in rats, based on bilateral manipulations of each site alone. The aim of the current investigation was to determine if the rBLA and plPFC function in a serial circuit to regulate cocaine-seeking during reinstatement testing.

**Methods:** An asymmetric rBLA-plPFC inactivation procedure coupled with unilateral rBLA and plPFC controls was used. Rats (n=6 per group) were initially trained to self-administer 1 mg/kg cocaine under a second-order schedule of reinforcement and stimulus cue presentation. After establishing stable baseline responding, rats underwent 3 weeks of response extinction training. Subsequently, lidocaine or vehicle was infused asymmetrically into the rBLA and contralateral plPFC or unilaterally into the rBLA or plPFC prior to a single reinstatement test with cocaine-paired cues.

**Results:** Analyses revealed that asymmetric lidocaine inactivation of the rBLA and contralateral plPFC blocked reinstatement of cocaine-seeking behavior relative to asymmetric vehicle control infusions (p< 0.05). As expected, unilateral inactivation of each site alone with lidocaine failed to disrupt reinstatement of cocaine-seeking behavior as compared to unilateral vehicle control infusions.

**Conclusions:** These findings support the proposed view of the rBLA as a critical component of reinstatement circuitry and suggest that the rBLA works in series with the plPFC to regulate cocaine-seeking behavior in the presence of cocaine-paired cues and absence of cocaine reinforcement. Retrograde tract tracing studies have revealed that the rBLA sends efferent projections to the plPFC (Hoover and Vertes, 2007), suggesting a neuroanatomical framework for interaction of these sites in regulating cue-induced reinstatement of cocaine-seeking behavior.

**Support:** Supported by DA 11716

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**METHYLPHENIDATE AS AN INTRAVENOUS REINFORCER IN RATS: INDIVIDUAL DIFFERENCES IN IMPULSIVITY PREDICT SELF-ADMINISTRATION.**

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**Aims:** In clinical literature, there is controversy about the abuse liability of methylphenidate among impulsive individuals and normals. Few studies have examined the reinforcing effect of methylphenidate (MPH) in laboratory animals. In rats, individual differences in behavior on a delay discounting task have predicted cocaine self-administration, with high-impulsive rats self-administering more cocaine than low-impulsive rats. In contrast no previous research has examined how differences in impulsivity affect MPH self-administration. The purpose of this experiment was to determine if intravenous MPH serves as a reinforcer in rats, and to examine how differences in impulsivity impact MPH self-administration.

**Methods:** Sprague-Dawley rats were exposed to a delay discounting procedure for 28 sessions. Lever pressing was then extinguished and rats were implanted with an intravenous catheter to assess self-administration of 0.56 mg/kg/infusion MPH. The FR value was increased from FR 1 to FR 5 across sessions. Self-administration rates of different MPH doses (0.03-1.0 mg/kg/infusion) were also examined. Then subjects were again exposed to 0.56 mg/kg/infusion MPH, followed by 0.56 mg/kg/infusion MPH presented non-contingently.

**Results:** All rats acquired MPH self-administration. Rats pressed more on the active lever than the inactive lever regardless of MPH dose and pressed more for MPH than for saline. The switch to non-contingent MPH administration decreased responding on the active lever. Differences in impulsivity on the delay discounting task were not correlated with differences in acquisition of MPH self-administration; however, rats that were high in impulsivity self-administered more MPH (0.1 mg/kg/infusion) than rats that were low in impulsivity.

**Conclusions:** MPH was shown to be a reinforcer when compared to responses on an inactive lever, saline self-administration, and non-contingent MPH administration. Delay discounting predicted self-administration of a low unit dose of MPH, suggesting that individuals who lack inhibitory control may be most susceptible to MPH abuse.

**Support:** USPHS Grants P50 DA05312 and T32 DA007304.

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**USE OF COMPLEMENTARY AND ALTERNATIVE THERAPIES AMONG METHADONE MAINTENANCE PATIENTS.**

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**Aims:** The aim of this study was to examine the prevalence of complementary and alternative medicine(CAM) use among methadone maintenance patients.

**Methods:** Data were collected as part of an ongoing study examining the effectiveness of a hepatitis care coordination model. Participants were 138 opioid dependent drug users recruited from two methadone maintenance clinics. Prevalence of ever using any CAM therapies, reasons for CAM use, perceived effectiveness of CAM use, and communicating with medical providers about CAM use were assessed.

**Results:** Participants were Caucasian (31%), African-American (29%), Latino (28%), and other (12%). The majority were male (64%), and the mean age was 47 (SD = 9.42). Of the 138 participants, almost all (99%) reported ever using at least one CAM therapy. The three most frequently reported therapies ever used included acupuncture/acupressure (42%), dietary supplements (40%), and religious healing (34%). The most frequently reported reasons for CAM use were to prevent health problems (43%), relaxation (37%), and pain management (33%). There was a high level of self-perceived effectiveness of CAM therapies (3.4 on a scale of 1-4). Participants also perceived that CAM therapies would be helpful adjunctive therapies for treating hepatitis C (46%), HIV (46%), and other chronic medical illnesses (67%). Approximately 10% sought information about CAM use from medical providers, and 15% reported that medical providers had recommended CAM therapy.

**Conclusions:** CAM use among methadone maintenance patients was prevalent. Methadone maintenance patients are knowledgeable about available CAM therapies, and perceive them to be effective in the prevention and treatment of medical conditions. Further investigations are needed to examine associations between CAM use and unmet health care needs.

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**PREDICTORS OF ALCOHOL INITIATION AMONG HISPANIC ADOLESCENTS IN PUERTO RICO.**

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**Aims:** Various social and psychological factors have been identified as significant correlates of alcohol use among adolescents. The goal of this study is to examine the predictors of alcohol use initiation among a cohort of Hispanic adolescents in Puerto Rico.

**Methods:** Participants were child (ages 12 to 15 years old) and his or her parents or caregivers (n = 693), recruited by outreach workers in randomly selected households within close proximity to drug markets. A list of 15 categories of psychoactive substances, alcohol and cigarettes was used to assess substance use. Analysis: Bivariate analyses were used to describe and examine the association between alcohol initiation and related characteristics. A multiple logistic regression model was fitted to identify the factors related to alcohol initiation among the group of adolescents.

**Results:** Overall, 87 (18.7%) adolescents had a first drink of alcohol during the first one-year follow-up. Adolescents 14 to 15 years old (27.1% vs. 12.2%), those that cut classes (31.7% vs. 14.2%), and who reported oppositional defiant disorder behavior (37.1% vs. 17.2%), involvement in violence (29.2% vs. 15.3%) and sexual behavior (40.7% vs. 16.7%) were more likely to initiate alcohol use than younger adolescents that did not engage in these non normative behaviors. Results of the logistic regression to alcohol initiation indicates that females, oldest adolescents (14-15), adolescents that cut classes, those involved in violent acts and with oppositional defiant disorder were more likely to initiate alcohol use. Access to cigarettes and drugs was variables related to adolescent alcohol use initiation.

**Conclusions:** Public policies that make alcohol less accessible and making already existing policies related to the selling of alcohol to minors more difficult. Organizations also need to help adolescents stay resistant to alcohol use initiation so that they may be able to finish their education in order to move upward in the socioeconomic social structure.

**Support:** This study was supported by NIDA Grant. Num. RO1 DA15301.

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**ROUTE OF ADMINISTRATION OF METHAMPHETAMINE: HOW IMPAIRED ARE SWALLOWERS?**

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**Aims:** To measure the levels of severity by route of administration. Previous research with smaller datasets has found injectors or smokers were the most impaired, with intranasal users (inhalers) less impaired. However, severity with oral administration (swallowers) does not appear to have been measured. This study examines which of the four routes of administration predict successively greater problems.

**Methods:** Methamphetamine users admitted into public programs in Texas (2003-2007) reported their primary route of administration and the number of days in the prior month they experienced problems with physical health, employment/school, family, social relationships, emotional, and drug/alcohol problems. Differences in the number of problems between selected pairs of groups [swallowers (n = 1,947) vs. inhalers (n = 3,878), inhalers vs. smokers (n = 17,623), and smokers vs. injectors (n = 13,114)] were assessed for persons under and over age 30 using negative binomial regression, with adjustments for race/ethnicity, gender, and other covariates.

**Results:** Among persons <30 years, swallowers compared to inhalers reported fewer days of employment/school problems, but no other significant differences were found; differences between inhalers and smokers were not found; smokers compared to injectors reported fewer days for all six problems. Among persons ≥30, swallowers compared to inhalers reported more days of emotional, social, and physical health problems; inhalers compared to smokers reported fewer days of drug/alcohol, employment/school, emotional, and social problems; smokers compared to injectors reported fewer days for all six problems.

**Conclusions:** This is the first study to compare all four routes of administration. While injectors consistently reported more problems than smokers, the findings for persons <30 provide little support for ranking swallowing below inhaling, or smoking above inhaling in terms of severity. Inhalers ≥30 reported fewer problems than smokers, but swallowers in this older group reported more problems than inhalers—an unexpected finding.

**Support:** University

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**MEASURING IMPULSIVE BEHAVIOR AND COGNITION IN INNER-CITY SUBSTANCE ABUSERS USING TRANSLATION PROCEDURES BASED ON PRECLINICAL RESEARCH.**

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**Aims:** Impulsive behavior (IMP-B) is widespread among substance abusers, and may contribute to abuse initiation and treatment compliance problems. Translational models of IMP-B can bridge between basic science and clinical application. The potential for using novel procedures based on animal studies to measure IMP-B and working memory (WM) was assessed in inner city psychiatric patients with or without substance abuse.

**Methods:** 31 psychiatric inpatients (19M, 12F, mean IQ 86.9) with diverse diagnoses were assessed using a computerized test battery including visual analog scales (VAS), the Barrett Impulsivity Scale (BIS), the Swedish University Scales of Personality, and 4 behavioral tasks: discrete trial N-back test of WM (Ko & Evenden, 2008), uncertain visual discrimination for reaction IMP, variable consecutive number test for ability to complete response sequences and a delay of reward task (Evenden, 1998, 1999, Evenden & Ryan, 1993). Patients were classified as +/- substance abuse (SA, 22/8), +/- history of legal problems (HoL, 13/18) and history of suicide (HoS, 20/11), and top 1/3rd & bottom 1/3rd on 5 measures of trait IMP and VAS state IMP. Data were analyzed with ANOVA and Bonferroni t-tests.

**Results:** +SA, +HoS and + HoL showed high trait IMP associated with high scores on SSP scales measuring anxiety, mistrust & irritability, but not IMP-B in the objective tests. High VAS state and BIS non-planning IMP were associated with improved performance on VCN (fewer short response chains). Subjects with +ve HoL made more errors on the WM test.

**Conclusions:** Self-reported trait IMP was associated with negative affect, suggesting that subjects' perception of their own behavior is influenced by affective context. The objective tests successfully eliminated this component, and there were few associations with self-rated IMP. Common neurobiological mechanisms underlie IMP-B and executive function and may become more important when affective load is minimized.

**Support:** Sponsored privately by JE and MM-E

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**EVIDENCE-BASED PRACTICES IN SUBSTANCE ABUSE TREATMENT: STAFF FAMILIARITY, OPINIONS, AND TRAINING.**

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**Aims:** Community-based providers face pressure to develop and employ continuous practice improvement strategies that are efficient, accessible and effective. The purpose of this project is to create a collaborative effort between the Richmond Behavioral Health Authority and its contracted community-based treatment providers to develop and pilot test a self-assessment protocol for practice improvement, designed to expedite the adoption of evidence-based practices (EBPs). Part of this assessment involves measuring staff opinions, use and training for various EBPs for substance use treatment.

**Methods:** Multi-level staff surveys were administered that assess, among other measures, staff use of and opinions about various EBPs.

**Results:** Preliminary analysis from 82 staff suggest differences in opinions between treatment staff and non-treatment staff on questions about the effectiveness of buprenorphine, the use of psychiatric medications, and the effect of incentives (all ps < .05). When asked about their use and familiarity with various EBPs, most licensed/certified staff (n = 31) reported using individualized drug counseling (97%), 12-step meetings (90%), intensive case management (90%) and client-centered therapy (90%), but had the least familiarity with cue-exposure (56%), clonidine (48%), nicotine replacement therapy (46%), the Matrix Model (46%), acamprosate (45%), and naltrexone (43%). However, few staff indicated that their organization had provided them with specific training in these areas. Most staff reported receiving training in methadone (70%), buprenorphine (76%), and cognitive behavioral therapies (61%).

**Conclusions:** Barriers to increasing the use of EBPs could include both discrepancies in opinions about EBPs, as well as inadequate training on EBPs. These findings indicate an opportunity to facilitate increased training on particular EBPs, across all types/levels of staff.

**Support:** This research was funded by NIDA R01DA022081-02

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### CHARACTERISTICS OF OPIATE INJECTION DRUG USERS WITH AND WITHOUT AMPHETAMINE TYPE STIMULATE ABUSE IN KUALA LUMPUR, MALAYSIA.

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**Aims:** Amphetamine type stimulant (ATS) abuse is on the rise in Malaysia and elsewhere in South East Asia. We evaluated the impact of ATS abuse on drug use patterns and HIV risk behaviors of opiate IDUs in Kuala Lumpur.

**Methods:** An anonymous survey of not-in-treatment IDUs (N=250) was conducted. Urine samples were tested for morphine, buprenorphine, methamphetamine, benzodiazepines and methadone before a structured, face-to-face interview was administered by trained RAs. Participants were paid 30 Ringgits (~\$8 USD).

**Results:** 224 (90%) males and 26 (10%) females were surveyed. The mean (SD) age was 38 (8). They were categorized as current ATS abusers (ATS+) if reporting  $\geq 1$  x/wk ATS use in the past month or testing positive on the methamphetamine urine test: 151 (60%) met these criteria, while 236 (94%) reported lifetime ATS abuse. Mean (SD) age of initiation of heroin and ATS use was 21 (5) and 33 (9) years, respectively. ATS+ were younger than those without current ATS abuse (ATS-) (37 vs. 39 years,  $p=0.08$ ) and less likely to be married (9% vs. 17%,  $p=0.04$ ). More ATS+ reported heroin as their primary drug of abuse rather than heroin and Suboxone (60% vs. 40%); the pattern was reversed for ATS- (60% reported both heroin and Suboxone as primary drugs of abuse,  $p=0.008$ ). No significant differences were found in education, employment, or benzodiazepine use. A higher proportion of ATS+ reported injecting drugs once per day or more (82% vs. 69%,  $p=0.014$ ) and having more than one current sexual partner (18.5% vs. 8%,  $p=0.02$ ).

**Conclusions:** The high prevalence and considerably more recent onset of ATS abuse (as compared to the onset of heroin use) in the study sample is consistent with reports of an emerging problem with ATS in Malaysia. ATS+ may be at increased risk for HIV transmission as a result of greater frequency of injecting drugs and higher sexual risk behaviors, supporting the importance of implementing interventions to reduce HIV risk behaviors in this population.

**Support:** Schering Plough SRT 4152 & K24 DA000445

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### IMPLEMENTATION OF MEDICATION ASSISTED TREATMENT IN MAINE AND MISSOURI: THE ADVANCING RECOVERY PROGRAM.

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**Aims:** Advancing Recovery uses systems change to promote implementation of evidence-based addiction treatments. This paper assesses implementation of medication assisted treatment in Maine and Missouri.

**Methods:** Process improvement tools facilitated state and provider system change. Maine and Missouri provided data on patients receiving medication assisted treatment. State and provider interviews described system changes and reactions.

**Results:** Maine modified regulations and contracts to require licensed addiction treatment programs to support medication. Counselor and physician training was provided. The state agency worked with Medicaid to prevent pre-authorization of buprenorphine and to add alcohol medications to the formulary. Use of buprenorphine increased nearly 500% between January – June 2006 (n = 39) (baseline) and January – June 2008 (n =192) in four treatment centers.

Missouri focused on access to alcohol treatment medications. Ten participating treatment centers adopted a screening tool to assess appropriateness for medication and trained counselors and physicians. The state authority modified contracts to reimburse medication costs and physician time. In the first year (October, 2006 – September, 2007) 170 patients received prescriptions for naltrexone or acamprosate; 61 patients were on active medication in September 2007. The contract and regulatory changes were extended statewide.

**Conclusions:** Maine and Missouri illustrate state and provider strategies for implementation of medication assisted treatment.

**Support:** Awards from the Robert Wood Johnson Foundation supported the state initiatives and a cross-site evaluation.

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### EFFECT OF COCAINE USE ON BUPRENORPHINE PHARMACOKINETICS IN HUMANS.

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**Aims:** The aims of this study were to determine 1) whether the pharmacokinetics of buprenorphine are affected by chronic cocaine abuse in those with a diagnosis of cocaine dependence, and 2) whether clinically significant pharmacokinetic or pharmacodynamic effects or toxicities occur when buprenorphine is used in the setting of cocaine dependence.

**Methods:** A retrospective analysis was done using data from prior studies of interactions between buprenorphine and antiretroviral medications. A total of 29 participants stably maintained on buprenorphine/naloxone 16/4 mg daily participated in 90 buprenorphine pharmacokinetics studies. Pharmacokinetics were compared for 74 studies completed on subjects who were not cocaine dependent and 16 studies on cocaine-dependent subjects.

**Results:** Participants with a diagnosis of cocaine dependence and regular cocaine use as indicated by consistently positive urine drug screens for cocaine metabolite had significantly lower buprenorphine exposure than other subjects (AUC 34% lower; Cmax 27% lower and Cmin 37% lower;  $p<0.001$  for all comparisons). Cocaine-dependent subjects showed a trend towards slightly higher concentrations of norbuprenorphine, and lower concentrations of buprenorphine glucuronide, although these differences were not statistically significant. Cocaine dependent individuals were younger ( $p=.0007$ ), more often met diagnostic criteria for cannabis abuse ( $p=.002$ ) or dependence ( $p=.001$ ), and used greater amounts of heroin ( $p=.004$ ) and cocaine ( $p<.0001$ ).

**Conclusions:** Cocaine abuse may result in lower buprenorphine plasma concentrations with potential for adverse clinical outcomes. Clinicians should screen opiate-addicted patients for cocaine dependence and provide treatment for both disorders when clinically indicated.

**Support:** Supported by NIH/NIDA RO1 DA 13004 (EMK), RO1 DA10100 (DEM) and K24 DA 023359 (EMK)

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### SMOKING ABSTINENCE INCREASES POSTERIOR INSULA-DEFAULT NETWORK FUNCTIONAL CONNECTIVITY.

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**Aims:** Smoking abstinence results in changes in spontaneous brain activity as measured by electroencephalography (Gilbert et al., 1999, 2004). Recently, fMRI and PET methods have elucidated correlated spontaneous brain activity in the absence of task demands in a network of midline structures including the precuneus and medial prefrontal cortex. This 'default network' likely reflects non-goal directed, introspectively-oriented cognition. The current study sought to evaluate the effects of smoking abstinence on the spatial distribution of this network using seed-based connectivity analyses.

**Methods:** BOLD-fMRI images were collected in a sample of smokers (n=19; mean cigarettes per day=17.08, SD=3.37) during a 5-minute eyes-closed resting period on two occasions: once following 24-hr abstinence and once following smoking as usual. Connectivity analyses were conducted with SPM5 using a seed in the precuneus (MNI: x=0, y=-56, z=30; 10 mm radius sphere).

**Results:** In each session, connectivity was observed between brain regions comprising the default network, though the extent of significant connectivity at FWE  $p<0.05$  was greater on the abstinent compared to satiated day (91488 v. 36328 mm<sup>3</sup>, respectively). When directly compared to the satiated condition, abstinence increased network connectivity in right posterior insula (MNI: 48,-6,-4) and decreased connectivity in left rostral anterior cingulate (MNI: -10,40,12).

**Conclusions:** The insula forms representations of internal bodily states and has been shown to subserve cigarette craving (Brody et al., 2002; Wang et al., 2007) and smoking (Naqvi et al., 2007). The present findings suggest the posterior insula—which receives and represents primary interoceptive information—is a component of the default network during the abstinent but not satiated state. These increases in posterior insula-default network connectivity in the abstinent state may reflect a shift to 'body-state-centered' cognition during withdrawal which in turn may bias smokers toward relapse.

**Support:** Research funded by a grant from the National Institute on Drug Abuse (K23DA017261; FJM).

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### REINSTATEMENT OF AMPHETAMINE SELF-ADMINISTRATION BY MDMA AND ITS ISOMERS IN RHESUS MONKEYS.

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**Aims:** The reinstatement paradigm is frequently used as a preclinical model of drug relapse. Typically drugs capable of inducing reinstatement share discriminative stimulus properties with the self-administered drug. 3,4-methylenedioxymethamphetamine (MDMA) is structurally similar to amphetamine and drug discrimination studies reveal that MDMA and amphetamine produce similar, although not identical, stimulus effects. Furthermore, drug discrimination studies with the isomers of MDMA generally indicate that S(+)-MDMA is more amphetamine-like than R(-)-MDMA. While discrimination studies have thoroughly characterized the stimulus properties of MDMA and its isomers, it is not known whether these compounds are capable of reinstating extinguished amphetamine self-administration. The present study was designed to compare the reinstatement effects of amphetamine, (+/-)-MDMA, S(+)-MDMA, R(-)-MDMA, and the piperazine-analogue BZP, in rhesus monkeys (n=4) maintained under a second-order schedule of i.v. amphetamine self-administration.

**Methods:** Following saline extinction, various doses of amphetamine, (+/-)-MDMA, S(+)-MDMA, R(-)-MDMA, and BZP were administered as non-contingent priming injections in order to characterize their ability to reinstate previously extinguished amphetamine maintained responding.

**Results:** Priming injections of amphetamine, (+/-)-MDMA and BZP induced robust, dose-dependent, reinstatement effects. In contrast, neither of the isomers of MDMA was effective in inducing reinstatement. The priming effects of (+/-)-MDMA, but not amphetamine or BZP, were attenuated by pretreatment with the serotonin transporter (SERT) inhibitor, fluoxetine.

**Conclusions:** The findings indicate that amphetamine, (+/-)-MDMA and BZP produce similar behavioral effects in the reinstatement paradigm, and suggest the priming effects of MDMA are mediated by a serotonergic mechanism, distinct from traditional psychostimulants.

**Support:** Supported by USPHS grants DA010344, DA000517 and RR00165.

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### SOURCES OF INCOME FOR CHRONIC DRUG USERS.

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**Aims:** To determine sources of income for chronic drug users (CDUs).

**Methods:** 600 CDUs of heroin and cocaine who were HIV negative were enrolled in a study to determine prevalence of risk factors for HIV. Participants were recruited from the "street" and completed a questionnaire using audio computer assisted interviewing (ACASI) technology. Demographic information was collected including sources of income and major source of income in the past 6 months. Drug use history and risk behaviors also were ascertained. Chi-square analysis was used to detect differences in sources of income between men and women.

**Results:** There were significant differences in the way in which men and women CDUs obtained income: job (26.4% vs. 10.1%); unemployment benefits (4.3% vs. .08%); spouse or sex partner (9.4% vs. 23.0%); family members (13.6% vs. 7.7%); prostitution (1.2% vs. 28.7%); and odd jobs (13.0% vs. 6.8%). There were no significant difference in obtaining income through VA, disability (5.4% vs. 9.3%); friends (21.0% vs. 25.8%); illegal sources (8.7% vs. 2.1%) and panhandling (9.6% vs. 4.6%). Among the men 8.5% reported having no income as did 4.4% of the women. Among those who reported income, the main source of income for men was a job (29.8%) while for women it was prostitution (26.8%).

**Conclusions:** There are significant differences in the way men and women CDUs obtain income. A job represented a small proportion of the methods used to obtain income and reliance on spouse, family, and friends was high as was prostitution among women. These data were collected at a time of high employment and a strong economy and these figures do not bode well for CDUs in the downturn of the economy. Many of the means used to obtain income such as panhandling, friends, and family are likely to disappear with the weak economy.

**Support:** NIDA grant RO1-DA-14231

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### STAFF REPORTS OF PROGRAM STRUCTURE IN RELATION TO CLIENT RETENTION, ALLIANCE, AND DRUG/ALCOHOL OUTCOMES.

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**Aims:** Treatment and client variables are associated with client engagement, retention, and outcome, only recently have studies examined program characteristics in relation to such outcomes. The goal of the current study was to examine clinicians' views of their organization in relation to client retention in treatment, therapeutic alliance, and drug/alcohol use in community-based substance abuse treatment clinics.

**Methods:** The study was conducted in 20 outpatient substance abuse treatment clinics in New York, Pennsylvania, Delaware, and New Jersey. Clinicians' (N=106) views of program characteristics were assessed using the Organizational Readiness for Change (ORC) measure, which has 18 scales organized into four major domains: staff attributes, motivation for change, program resources, and organizational climate. Clients (N=986) currently in treatment reported on their current length of treatment, quality of therapeutic alliance with their clinician, treatment satisfaction, and weekly drug/alcohol use.

**Results:** Clinicians' ratings of staff attributes of efficacy (r=.19, p=.05) and adaptability (r=.23, p=.02) were significantly correlated with patients' ratings of therapeutic alliance. Motivation for change, as reflected in program needs (r=-.25, p=.0096) and pressures for change (r=.19, p=.046), was significantly related to average treatment length and frequency of patient alcohol use, respectively. In terms of program resources, clinicians' perceptions of the adequacy of agency staffing was significantly (r=.21, p=.03) related to patients' ratings of treatment satisfaction. The organizational climate dimension of stress was significantly related to alliance (r=-.23, p=.016) and treatment satisfaction (r=-.21, p=.03). All correlations were in the expected direction.

**Conclusions:** Program characteristics, as rated by clinicians, are associated with patient alliance, treatment satisfaction, treatment length, and alcohol use in substance use treatment clinics.

**Support:** (NIDA R01 DA020809-01 & R01 DA020799)

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### AMYGDALA VOLUMES IN ADOLESCENT MARIJUANA USERS.

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**Aims:** Converging evidence indicates potential vulnerability to neurotoxic effects of marijuana (MJ) among adolescents. The amygdala has been implicated in the onset and maintenance of addiction as a center for processing reward-driven and withdrawal-avoidant behaviors. Densely populated with cannabinoid receptors, the amygdala may be more susceptible to neural changes induced by chronic MJ use during adolescence. Here, we examined amygdala volumes in adolescent MJ users and explored potential gender differences.

**Methods:** Participants (ages 16-19) were 26 MJ teens and 19 demographically similar controls. Exclusions included psychiatric or neurologic disorders, prenatal substance exposure, excessive polysubstance use, left-handedness, pregnancy and psychotropic medicine. Amygdala volumes were obtained by manual tracing of reliable raters (ICCs>.85) on high resolution MRIs. Multiple regressions examined whether amygdala volumes were associated with MJ use status alone or in interaction with gender.

**Results:** After controlling for intracranial volume, age, gender, alcohol and cigarette use, MJ teens did not exhibit different amygdala volumes (left, right or total) than controls (f2 effect sizes ranged .026-.003). No interactions between group and gender were found (f2 range .03-.004). Duration of regular alcohol use was marginally associated with larger left amygdala volumes (p<.06). Secondary analysis demonstrated that amygdala morphometry was not linked with family history of substance use disorders or mood symptoms.

**Conclusions:** Preliminary results suggest a lack of relationship between heavy adolescent MJ use and amygdala size. This is surprising given our prior findings of larger prefrontal cortex volumes in female users and larger vermis volumes in similar samples, but present results may indicate that limbic regions are not similarly affected by MJ exposure during adolescence. Longitudinal studies, currently underway, will determine whether adverse effects on amygdala morphometry are seen as these heavy MJ-using teens transition into young adulthood.

**Support:** NIDA DA021182 (Tapert) & DA020206 (Medina)

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**ATOMOXETINE IN MARIJUANA-DEPENDENT ADULTS WITH ADHD.**

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**Aims:** Attention deficit hyperactivity disorder (ADHD) commonly co-occurs in patients with marijuana use disorders. This double-blind, placebo-controlled study was conducted to explore the efficacy of atomoxetine in marijuana-dependent adults with ADHD.

**Methods:** Subjects received atomoxetine (maximum 100 mg/day) (n=19) or placebo (n=19) for 12 weeks. Subjects were between 18 and 65 years of age and met DSM-IV criteria for marijuana dependence and ADHD. Exclusion criteria included other substance dependence (except nicotine), and major medical or psychiatric illnesses. Marijuana use for the 90 days prior to study entry was estimated using the Time-Line Follow-Back (TLFB). TLFB data and urine drug screens (UDSs) were collected weekly throughout the study. The Wender Reimherr Adult ADHD Scale (WRAADS) was used to assess ADHD symptoms, and the Clinical Global Impression (CGI) scale was used to assess ADHD and substance use improvement. Subjects also participated in motivational enhancement therapy sessions.

**Results:** A total of 272 evaluable UDSs were obtained from the 38 subjects. Atomoxetine was not found to decrease the odds of a positive UDS in a generalized estimating equations (GEE) model ( $p=0.83$ ). Likewise, no statistically significant treatment by time interaction was found for a longitudinal model examining rates of change in weekly mean TLFB-reported use ( $p=0.20$ , GEE/robust variance estimator). Groups did not differ on a CGI rating for marijuana improvement (Wilcoxon Rank Sum;  $p=0.64$ ); however, subjects randomized to atomoxetine had greater improvement in ADHD symptomatology than placebo subjects on the CGI (WRS;  $p=0.016$ ). The WRAADS rating suggests a greater rate of decline in ADHD symptoms for the atomoxetine subjects over the first 4 weeks ( $p=0.028$ ), but treatment by time interaction was not significant after week 4.

**Conclusions:** Atomoxetine demonstrates preliminary efficacy for ADHD symptomatology in comorbid substance use disorder, but does not appear to improve marijuana use outcomes.

**Support:** Supported by R21DA18221 (McRae-Clark) and K24DA00435 (Brady).

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**CHARACTERISTICS OF PSYCHOPATHY IN ADOLESCENT NONSMOKERS AND SMOKERS: RELATIONS TO DELAY DISCOUNTING AND SELF REPORTED IMPULSIVITY.**

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**Aims:** This research compared impulsive behavior in adolescent nonsmokers with low ratings of psychopathy ( $n = 25$ ) and daily smokers with low ( $n = 25$ ) and high ( $n = 25$ ) ratings of psychopathy. It was expected that the high psychopathy smoker group would rate highest on measures of impulsivity, followed by the low psychopathy smoker group, and followed by the nonsmoker low psychopathy group. This would indicate an additive effect of cigarette smoking and psychopathy on impulsivity.

**Methods:** Assessments of impulsive behavior included question-based and real-time measures of delay discounting and a self report assessment of impulsivity (Barratt Impulsiveness Scale-Adolescent).

**Results:** Overall group differences were explored using two-way Analyses of Variance and significant interactions were examined using LSD post-hoc analyses. Smokers with low psychopathy ratings discounted more by delay (i.e., more impulsively) than nonsmokers on both assessments of discounting ( $p = .010$  and  $.006$ , respectively); however, smokers with high psychopathy ratings did not differ from nonsmokers on either measure ( $p = .390$  and  $.958$ , respectively). Inversely, from the self report assessment of impulsivity, smokers with low psychopathy ratings did not differ from nonsmokers ( $p = .444$ ), but smokers with high psychopathy ratings were more impulsive than nonsmokers ( $p = .018$ ).

**Conclusions:** These findings indicate that delay discounting and self reported impulsivity relate differently to characteristics of psychopathy in adolescent nonsmokers and smokers. Also, these findings demonstrate that there are definable subgroups of smokers for whom the frequently observed relationship between cigarette smoking and delay discounting does not apply. This finding was unexpected and is inconsistent with what has been a reliable outcome in the delay discounting literature.

**Support:** Support for this research was provided by two research awards from the Social and Behavioral Sciences Department and by an award from the Arts and Sciences Department, The Ohio State University.

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**FMRI BRAIN ACTIVATION DURING A DELAY DISCOUNTING TASK IN HIV-POSITIVE ADULTS WITH COCAINE DEPENDENCE.**

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**Aims:** Cocaine users tend to choose smaller, immediate rewards over larger, delayed ones. The co-occurrence of HIV/AIDS and drug abuse has deleterious effects on cognitive and neurological functioning. This study examined the effect of cocaine dependence on brain activity during a delay discounting task in HIV-positive adults.

**Methods:** Participants were 36 HIV-positive adults on antiretroviral therapy who had current cocaine dependence ( $n=12$ ), past cocaine dependence ( $n=13$ ), or no history of substance use disorder ( $n=11$ ). Participants completed a delay discounting task, followed by a modified version during fMRI scanning.

**Results:** Participants were 69% male, 27-58 years old, and ethnically diverse. They were diagnosed with HIV 3-26 years ago, and 64% had AIDS. The mean discount rate was .064, .033, and .028 for active, recovered, and non cocaine users, respectively; there was no difference between active and recovered/non cocaine users ( $t(37)=0.97$ , ns). However, cocaine users had greater change in their discount rate over time (.085 versus .016;  $t(19)=3.49$ ,  $p<.01$ ). During the fMRI task, there were significant group differences during "hard" versus "no choices" in the right orbitofrontal cortex and precentral gyrus and bilaterally in the cerebellum, thalamus, anterior cingulate gyrus, occipital cortex, pallidum, and putamen. Many of these regions are known to be involved in decision-making processes.

**Conclusions:** There was large variability in discount rates in this HIV-positive sample, with cocaine users demonstrating greater change over time. Current cocaine users also evidenced differences in neurobiological functioning when making difficult choices between less money today versus more later. These patterns in responding may contribute to impulsive decision making, with implications for health risk behaviors, and individuals who have HIV/AIDS and cocaine dependence may be at greater risk.

**Support:** American Foundation for AIDS Research (106884-42-RFBR), Harvard Center for AIDS Research (P30-AI-60354), National Institute on Drug Abuse (T32-DA-015036)

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**IMPACT OF THE DRUG USE AND SUBSTITUTION TREATMENTS ON THE ANTIVIRAL TREATMENT OF CHRONIC HEPATITIS C ANALYSIS OF ADHERENCE, VIROLOGICAL RESPONSE AND QUALITY OF LIFE (CHEOBS).**

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**Aims:** CHEOBS is a French prospective, observational study that aimed to analyze the factors associated with adherence with to treatment by peginterferon alfa-2b and ribavirin in chronic hepatitis C patients. The present analysis focuses on virological response, quality of life according to whether the patients were active drug users or under substitution treatment (ADU), ex-drug users (EDU), or non-drug users (NDU).

**Methods:** Between 2003 and 2006, 184 clinicians evaluated 2001 patients every 3 months during treatment, and 6 months after the end. 141 were excluded: the studied population included 244 ADU, 578 EDU, and 1038 NDU. Of the 244 patients ADU, 72 were receiving methadone therapy and 137 buprenorphine. Good compliance was defined by >80% of the dose and duration of the antiviral therapy prescribed. Sustained virological response (SVR) was defined by a negative PCR  $\geq 12$  weeks after the end of treatment. QoL was assessed using the SF-36 questionnaire.

**Results:** The patient profile in the EDU group was between that in the ADU and NDU groups for mean age, body mass index, liver fibrosis, level of education, high consumption of alcohol, psychiatric disorders, or chronic diseases. The proportion of good adherers to patients with therapy was similar in all three groups: NDU 49.4%; EDU 48.6%; ADU, 52.2% ( $p=0.7$ ). The SVR rate was also similar: 49.3%, 50.9%, and 57.8% respectively ( $p=0.1$ ). The QoL in the ADU group was less altered on the physical and psychological levels than in patients in the other groups.

**Conclusions:** The rate of SVR was similar in the three groups. Excess consumption of alcohol, a precarious socioeconomic situation, and the psychiatric disorder observed in drug users in this study did not have negative impact on the treatment outcome. On the contrary, young age, recent contamination, high prevalence of genotype 3 infection, less severe liver fibrosis, and good adherence to treatment seem to have balanced the negative parameters.

**Support:** Schering plough

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# IDENTIFYING PRESCRIPTION DRUG DISORDER IN PRIMARY CARE CHRONIC PAIN PATIENTS PRESCRIBED OPIOIDS: DIAGNOSTIC CHARACTERISTICS OF THE CURRENT OPIOID MISUSE MEASURE.

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**Aims:** Aims: The Current Opioid Misuse Measure (COMM), a self-report assessment of past-month aberrant medication-related behaviors (AMRBs), has been validated in specialty pain management patients. We determined the performance characteristics of the COMM in primary care (PC) patients with chronic pain receiving prescription opioids. We hypothesized that the COMM can identify patients with prescription drug disorder (PDD) and distinguish them from those with other substance use disorders (SUDs) or no disorder.

**Methods:** Methods: Subjects were English-speaking patients (ages 18-60) with chronic pain ( $\geq 3$  months), who received  $\geq 1$  opioid analgesic prescription in the past-year and were awaiting PC visits at an urban, safety-net hospital. The Composite International Diagnostic Interview (CIDI) was the "gold standard", defining a DSM-IV diagnosis of past-year PDD and other SUDs. Past-month AMRBs were assessed with the COMM. A receiver operating characteristics (ROC) curve demonstrated the COMM's diagnostic test characteristics.

**Results:** Results: Of 238 participants, 27 (11%) met DSM-IV PDD criteria, while 17 (7%) had other SUDs, and 194 (82%) had no disorder. The mean COMM score was higher in those with PDD than among all others (i.e., those with other SUDs or no SUD) (mean 20.4 [SD 10.8] vs. 8.4 [SD 7.5]),  $p < 0.0001$ . Sensitivity and specificity were 80% and 71%, respectively, for a COMM score of  $\geq 12$ , and 76% and 76% for a score  $\geq 13$  for identifying patients with PDD. The area under the ROC curve was 0.84.

**Conclusions:** Conclusions: Among PC patients with chronic pain receiving prescription opioids, the COMM appears to be able to identify patients with PDD and distinguish them from all other patients, including those with other SUDs. For PC physicians treating chronic pain patients prescribed opioids, the COMM may be a promising tool for identifying an often-feared complication, the development of PDD.

**Support:** Supported by K23 DA016665

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# PATTERNS OF ALCOHOL CONSUMPTION AMONG COLLEGE FOOTBALL TAILGATERS.

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**Aims:** To examine patterns of alcohol consumption among spectators at college football tailgating activities.

**Methods:** Participants were 258 individuals (56.4% male) aged 18-71 years (M = 28.62 years, SD = 10.49). Investigators approached on-campus tailgaters from 2 ½ hours before kick-off until 10 minutes after kick-off before two home football games (one starting at 1:30pm [n = 119] and one starting at 8:00pm [n = 139]). After providing consent, participants completed a short interview and submitted a breath sample. The Intoximeter Alco-Sensor IV was used to estimate BAC.

**Results:** About 71% of participants reported that they would be attending the game. Those under 21 (n = 20) reported consuming between 0-20 alcoholic beverages at the time of their interaction with the investigators (M = 2.63, SD = 5.59), with estimated BAC levels ranging from 0.00 to 0.22 (M = 0.02, SD = 0.06); whereas, individuals 21 and over (n = 238) reported consuming between 0 to 25 drinks (M = 4.99, SD = 4.18) and had estimated BAC levels ranging from 0.00 to 0.31 (M = 0.08, SD = 0.07). There was a significant difference between groups on self-reported consumption ( $t = -2.36$ ,  $p < .02$ ) and estimated BAC ( $t = -3.81$ ,  $p < .001$ ). In total, 40.2% of participants produced breath samples over the legal limit for driving (i.e., 0.08 or higher). There was a significant difference in self-reported consumption between males (M = 6.25, SD = 4.71) and females (M = 2.95, SD = 2.90;  $t = 6.93$ ,  $p < .001$ ). Males (M = 0.09, SD = 0.07) also produced significantly higher estimated BAC levels than females (M = 0.05, SD = 0.06;  $t = 4.60$ ,  $p < .001$ ).

**Conclusions:** Alcohol consumption is a significant part of pre-football game "tailgating" festivities. More effort is needed to promote safety and decrease binge drinking at these events.

**Support:** This study was sponsored by the University of Florida Department of Psychiatry.

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# THE EFFECTS OF SUBLINGUAL SALVINORIN A, A NATURALLY OCCURRING KAPPA OPIOID RECEPTOR AGONIST, IN HUMANS.

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**Aims:** Salvia divinorum (SD) is an unregulated plant-based drug (estimated 1.8M US lifetime users). Most users smoke dried leaf fortified with plant extract. The primary psychoactive compound is thought to be Salvinorin A (SA), a selective kappa receptor opioid agonist. Because SA is a relatively new drug there are no data on human effects; this is the first report of a controlled study of SA in humans.

**Methods:** In this ascending-dose, placebo-controlled study, 8 SD-experienced subjects received sublingual doses of 100-4000 µg SA. Instead of inhaled dosing, sublingual dosing was studied to make bioavailability more consistent. Outcome measures included Likert-scale questionnaires and visual analog items (e.g., intoxication, good drug, bad drug, headache, and nausea). A sensitive and specific LC/MS/MS plasma assay for SA and Salvinorin B (SB, the major metabolite of SA) was developed, and plasma obtained at 20 and 40 min post dose.

**Results:** Self-report results are available for 6/8 subjects; plasma for 1 subject in this ongoing study (full results will be presented at the conference). Sublingual SA produced variable effects. While most subjects reported negligible effects, one subject had brief modest intoxication (VASintox 35 at 15 min). Plasma SA levels in this subject were 0.338 ng/mL and 0.173 ng/mL at 20 and 40 mins, which, while detectable, were below the reliable level of quantification. SB was quantifiable with levels of 0.921 and 0.649 ng/mL at 20 and 40 mins.

**Conclusions:** Effects produced with these doses and this route were lower than those normally experienced by participants when smoking SD. Sublingual effects may be limited because of low bioavailability due to the poor water solubility of SA. Both SA and SB can be detected in plasma with a sensitive LC/MS/MS assay.

**Support:** Supported by a private donation.

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# CONCURRENT TREATMENT OF SUBSTANCE USE DISORDER AND POST TRAUMATIC STRESS DISORDER: A TREATMENT THAT WORKS FOR BOTH GENDERS?

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**Aims:** Rates of Post Traumatic Stress Disorder (PTSD) in people with substance use disorders are 6.5 times that of the general population. Those with this comorbidity pose a challenge to treatment providers, however, treatment options for this comorbidity are scarce and many have been designed to treat either men or women specifically. These options have also been poorly researched. A randomized controlled trial of an integrated treatment for both disorders targeting both genders is currently being conducted in Australia. This paper presents case-control comparisons of two females and two males – one participant of each gender pair randomized to COPE and one randomized to treatment as usual.

**Methods:** The integrated intervention, Concurrent Treatment with Prolonged Exposure consists of 13, 90-minute psychotherapy sessions and is based on cognitive-behavioral therapy and includes exposure based techniques. Outcome data is obtained by comprehensive assessments at baseline, 6 wks, 3 and 9 mths follow-up.

**Results:** Comparisons between treatment and control participants showed that while treatment participants reported no substance use at follow-up points, the control participants were not able to maintain some of the earlier changes they made regarding their substance use over the follow-up period. In addition, the treatment participants did not meet diagnostic criteria for PTSD at all follow up stages compared to control participants who met PTSD diagnosis throughout the assessment period.

**Conclusions:** These findings provide preliminary support for the efficacy of the concurrent treatment of PTSD and substance use disorders using COPE and suggests that this treatment is suitable for both genders.

**Support:** This research project was supported by the National Health and Medical Research Council, Australia.

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# EXPRESSIVE WRITING AS A THERAPEUTIC ADJUNCT TO TREATMENT FOR DRUG-DEPENDENT WOMEN: SHORT-TERM OUTCOMES FROM A RANDOMIZED CLINICAL TRIAL.

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**Aims:** The present study compared short-term (2 week) outcomes in a RCT comparing expressive writing to a control condition in a sample of 141 women in residential drug treatment. The relationships among trauma, depression and levels of psychiatric distress at baseline were also compared.

**Methods:** The sample was predominantly African-American (68.1%) with mean age of 36.4 yrs and mean education of 10.9 yrs. Women were recruited following admission to drug treatment and completed baseline measures including: Posttraumatic Stress Diagnostic Scale (PDS), CES-Depression Scale (CES-D), and Brief Symptom Inventory (BSI).

**Results:** Nearly 95% of women reported at least one lifetime trauma and 54.6% met diagnostic criteria for current (past month) PTSD. SUD women with PTSD reported greater anxiety distress (raw score  $M = 1.4$ ) compared to those without PTSD (raw score  $M = 0.6$ ) ( $F(139) = 14.2$ ,  $p < .0001$ ). Women with elevated CES-D depression scores also reported greater trauma symptom severity compared to those with non-elevated scores. In a preliminary analysis of short-term RCT outcomes at 2 weeks post-intervention, a multivariate general linear model examined between group differences from baseline to 2 week follow-up on CES-D and BSI scores. Women randomized to expressive writing had a significantly greater decrease in depression levels from baseline to follow up as compared with those randomized to the control group ( $F(103) = 4.3$ ,  $p < .05$ ). Further, women randomized to expressive writing had a significantly greater decrease in BSI anxiety levels from baseline to follow up compared with those of the control group ( $F(103) = 7.9$ ,  $p < .01$ ).

**Conclusions:** Findings suggest that expressive writing may be a clinically and economically useful adjunct to standard SUD treatment for women with trauma.

**Support:** Research supported by VCU Institute for Women's Health and NIDA R36 DA024021

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# PERSISTENCE OF COCAINE USE ONCE IT STARTS: INITIAL FINDINGS FROM EPIDEMIOLOGICAL RESEARCH.

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**Aims:** An estimated 5%-6% of cocaine users develop a cocaine dependence syndrome within 1-2 years after onset of first cocaine use in a process that starts with an increasing number of days of cocaine use that drives, and is driven by, a drug dependence process. In this large-sample epidemiological research, we seek a more complete understanding of population sub-group variation in persistence of this cocaine process, with a focus on male-female and race-ethnicity variation in the experience of recent-onset cocaine users (ROCU), defined to include individuals who started cocaine use within 24 months of field survey assessment.

**Methods:** Data are from 621 ROCU self-identified among the 55,279 National Survey on Drug Use and Health participants who completed confidential computer-assisted self-interviews in 2006. Analyses of sub-group variation are based upon a Poisson count regression model for the frequency of cocaine use in the month just prior to the date of assessment, with due attention to NSDUH sample design and weights.

**Results:** Male and female ROCU did not differ ( $p > .05$ ), but increasing age had a non-linear relationship with persistence of cocaine use among ROCU ( $p < .05$ ). In addition, with age (and sex) held constant, there was noteworthy race-ethnicity variation in persistence of cocaine use ( $p < .05$ ). For example, ROCU in the Native American/Alaskan Native subgroup had an exceptionally low frequency of recent cocaine use, as compared to non-Hispanic Whites and other race-ethnicity sub-groups.

**Conclusions:** As manifest in the number of days of recent cocaine use among these recent-onset cocaine users, the process of cocaine involvement is one that shows no male-female variation, but there is noteworthy and statistically robust variation in relation to age and race-ethnicity, which merits more detailed inquiry.

**Support:** NIDA award K05DA015799 & T32DA021129.

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# DOES CRACK COCAINE INCREASE SEXUAL DESIRES? PERCEPTIONS OF HIV-POSITIVE CRACK COCAINE USERS AND GENDER DIFFERENCES.

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**Aims:** Previous research has suggested that crack cocaine users are at risk for sexual transmission of HIV due to the "hypersexuality" associated with crack use. Few studies have examined crack users' perceptions of how crack affects their sexual desires and whether they are associated with risky sexual behaviors.

**Methods:** Interviews were conducted with 281 HIV-infected crack cocaine users who were admitted to two inner city hospitals in Miami, FL and Atlanta, GA between 2006 – 2008. Multivariable analyses assessed variables associated with participants who reported that crack use helped/increased their sex drive.

**Results:** The study sample was 53% female, 72% was over the age of 40, and 90% was African American. Overall, participants said that crack use helped (19%), hurt (36%) or had no effect (31%) on their sex drive and 14% said that the effect was different every time. Males were more likely to report crack helping their sex drive (26% of males vs. 12% of females). Females were more likely to report crack hurting their sex drive (45% of females vs. 24% of males). In multivariable analysis, females (AOR .281, CI .126, .627) had decreased odds for reporting that crack helps one's sex drive. There was an interaction between gender and anal sex (AOR 4.923, CI 1.12, 21.71) with females who had anal sex having 5 times increased odds for reporting that crack helps one's sex drive.

**Conclusions:** A small minority of crack users reported that use helps their sexual desire, raising questions about previous reports on "hypersexuality" associated with crack use. Notably, there is a gender difference that needs further exploration as it appears that crack is more likely to serve as a sexual stimulant for men than women except for women who report engaging in anal sex. Further research is needed to explore how crack use affects sexuality and how these beliefs can be considered in the development of interventions that address prevention of HIV transmission.

**Support:** National Institute on Drug Abuse

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# SAFETY OF ORAL ARIPIPRAZOLE ALONE AND IN COMBINATION WITH INTRAVENOUS COCAINE IN HUMANS.

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**Aims:** Aripiprazole (ARP), an atypical antipsychotic, acts as a partial dopamine agonist and may be an effective pharmacotherapy for cocaine dependence. This inpatient laboratory study is examining the efficacy of ARP to reduce the subjective and reinforcing effects of cocaine. Interim safety data are presented.

**Methods:** Healthy adults using cocaine (2-3x/week) enrolled in this double-blind, placebo-controlled, mixed-design study. A placebo lead-in (~7 days) was followed by randomization to ARP (0, 2 or 10 mg, p.o./day) for ~23 days. Cocaine challenge sessions (0, 20 & 40 mg/70kg, i.v. 1 hr apart in ascending order) were conducted during placebo lead-in and twice after randomization. Safety measures included lipids, blood glucose, weight, extrapyramidal side effects, QTc, heart rate (HR) and blood pressure.

**Results:** Mean weight increased significantly (17.6 lbs) over the 1-month study and was accompanied by an increase of 30 mg/dL in total cholesterol ( $p < .05$ ), but there were no group differences. There were no significant increases in fasting blood glucose or ECG QTc as a function of group or time. There was no change in baseline HR in the placebo group, while maintenance on 2 and 10 mg ARP produced sustained increases. Systolic and diastolic blood pressures were also increased by both ARP doses over time. Cocaine administration produced expected increases on blood pressure and pulse; despite the direct actions of ARP on these indices, there was no evidence of synergistic cardiopressor effects in the presence of cocaine. All ARP and cocaine dose combinations were safely tolerated, and there was no evidence of extrapyramidal signs or symptoms.

**Conclusions:** This interim safety evaluation revealed that ARP was generally well tolerated by these healthy individuals with cocaine abuse histories. However, direct cardiovascular effects of ARP were observed that, while not of clinical significance in this cohort, could be potentially problematic in the general population of stimulant abusers in uncontrolled settings.

**Support:** NIDA DA019433(SLW)

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**TEMPORAL AND PROBABILISTIC DISCOUNTING IN ADOLESCENT SUBSTANCE USERS AND CONTROLS.**

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**Aims:** When choosing between delayed or uncertain outcomes, individuals discount values of outcomes based on the expected time to, or likelihood of, their occurrence. Similar hyperbola-shaped mathematical functions have been used to describe temporal discounting (TD) and probabilistic discounting (PD) of rewards, suggesting that similar processes might underlie them. TD studies have repeatedly shown that adults discount smaller rewards more rapidly than larger rewards and that substance using (SU) adults discount delayed rewards more rapidly than controls. PD results have been less consistent, with some suggesting no effect or the opposite effect of reward magnitude and that PD rates might not be greater in substance users. We hypothesized that large probabilistic rewards would be discounted more rapidly in adolescents and that aspects of PD might differ for SU adolescents.

**Methods:** Forty SU adolescent patients and 40 controls completed computerized tasks assessing TD and PD for \$40 and \$500 rewards. Nonlinear mixed models incorporating random rate parameters and multivariate responses evaluated reward magnitude within-subjects and between groups for delay and probabilistic tasks.

**Results:** For both large and small rewards, SU patients discounted delayed rewards more rapidly than controls ( $p < 0.05$ ). However, discounting rates did not differ between groups for probabilistic rewards. Multivariate models indicated that both SU patients and controls discounted smaller delayed rewards more rapidly than larger rewards ( $p < .05$ ) but neither group demonstrated a magnitude effect in PD.

**Conclusions:** Temporal discounting processes in adolescents with and without substance use problems were similar to those reported in adults, with both groups exhibiting magnitude effects and with SU patients discounting delayed rewards more rapidly than controls. Although discounting of probabilistic rewards was similarly modeled, there were no differences in magnitude or between groups, suggesting important differences between TD and PD processes.

**Support:** NIDA DA011015 & DA009842

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**WHAT IS BEST PRACTICE IN THE TREATMENT OF CO-OCCURRING SUBSTANCE USE AND POST TRAUMATIC STRESS DISORDER?**

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**Aims:** This paper aims to provide a review of the literature pertaining to the pharmacological and psychological treatment of co-occurring substance use and post traumatic stress disorder

**Methods:** A systematic literature review was conducted on the following databases: Pubmed, PsychInfo, Medline, EMBASE and CINAHL. The following terms were searched to identify studies relevant to the treatment of co-occurring substance use and PTSD: "post traumatic stress disorder"; "post-traumatic stress disorder"; "posttraumatic stress disorder"; "PTSD"; "substance"; "drug"; "alcohol"; "abuse"; "dependence"; "treatment" as the key search terms.

**Results:** The evidence base regarding the treatment of co-occurring substance use and PTSD is limited. Only two studies have examined the use of pharmacotherapy in this population, both of which investigated the use of sertraline. The results do not conclusively support or refute the use of sertraline in the treatment of this comorbidity. Research into psychotherapies has been somewhat more extensive, however, studies have been limited by small sample sizes, lack of a control condition, and short follow-up periods. To date, only one psychotherapy has been evaluated in a large randomised controlled trial. Despite these limitations, the evidence provides promising support for the use of psychotherapies in the treatment of substance use and PTSD.

**Conclusions:** Evidence regarding the treatment of co-occurring substance use and PTSD is sparse. Nonetheless, that which does exist suggests that co-occurring PTSD can be successfully treated among substance users. However, further research is required to determine how best this may be achieved.

**Support:** This review was conducted as part of a randomised controlled trial of an integrated treatment for substance use and PTSD, funded by the Australian National Health and Medical Research Council

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**PAIN-ELICITED AND -SUPPRESSED BEHAVIORS IN CB1 KNOCKOUT MICE AND THEIR WILD-TYPE LITTERMATES: EFFECTS OF MORPHINE.**

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**Aims:** The present study utilized CB1 cannabinoid receptor knockout mice (CB1 KO) and their wild-type littermates (CB1 WT) to examine behaviors elicited by thermal (hotplate assay) and visceral noxious stimuli (acetic acid induced writhing), and suppressed by visceral noxious stimuli (acetic acid suppressed food consumption). The effects of morphine were determined.

**Methods:** In the hotplate assay, mice were tested across a range of temperatures (44° to 56° C), and the effects of morphine (1.0-32.0 mg/kg) were assessed at 56° C. For experiments using acetic acid, mice were food (12 hr) and water (2 hr) deprived prior to the test session. On the test day, mice were given an injection of saline or morphine (0.32-10.0 mg/kg, s.c.) 45 min prior to the session and an injection of saline or 0.56% acetic acid (i.p.) immediately prior to the session. The number of writhes and levels of consumption of 32% Liquid Nutrition (CVS®) were measured over 30 min.

**Results:** CB1 WT and CB1 KO did not differ on the hotplate at any temperature; however, exposure to 0.56% acetic acid produced significantly more writhes in CB1 KO ( $28.33 \pm 4.14$ ) than in CB1 WT ( $15.33 \pm 4.06$ ). Baseline consumption was greater in CB1 WT ( $0.09 \pm 0.005$  g/g) than CB1 KO ( $0.05 \pm 0.007$  g/g), but exposure to acetic acid resulted in similar decreases in consumption in both genotypes. Pretreatment with morphine increased hotplate latencies and inhibited writhing in both genotypes, but did not significantly attenuate the suppression of feeding by acetic acid in either genotype.

**Conclusions:** These data suggest a role of the cannabinoid system in the writhing response to injection of acetic acid, but not in the response to thermal noxious stimulation in the hotplate assay. In addition, these data are consistent with other research suggesting a role for the cannabinoid system in the consumption of palatable foods (Ward and Dykstra 2005). Morphine had similar effects in CB1 WT and KO mice in both assays of pain-elicited behavior but did not significantly alter pain-suppressed food consumption.

**Support:** R01-DA002749 and T32-DA007244.

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**EFFECT SIZE, TIME AND DOSE RESPONSE PROFILES OF DRUGS OF ABUSE IN HUMAN ABUSE POTENTIAL STUDIES.**

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**Aims:** Human abuse potential is evaluated in crossover studies where single test drug doses are compared to placebo and scheduled active control(s). Study interpretation should rely on 'clinically important' differences to ascertain abuse potential for novel drugs; however, the typical size of such an effect is not established. We report response patterns on abuse potential measures for various doses of CII-IV drugs.

**Methods:** Combined data from 14 single-dose, randomized, double-blind, placebo-controlled, crossover studies are summarized using percentage (%) peak effect differences from placebo. History and pharmacologically qualified healthy adult recreational drug users (combined N>350) performed measures using 21CFR11 validated software (Scheduled Measurement System).

**Results:** Differences from placebo for Drug Liking and Good Effects visual analog scales (VAS) were typically >30% while differences <20% were observed for very low or high doses of some drugs (e.g., 4 mg hydromorphone, 4 mg alprazolam). Other than ketamine and high dose sedatives, differences for Bad Effects VAS were <30%. Dose-response effect sizes were not necessarily larger for stimulants/opioids, but were more pronounced than for sedatives/ketamine. Time course effect differences also contribute to abuse potential. The bipolar Drug Liking VAS was as sensitive as unipolar scales (e.g., Good Effects), had lower variation, was less susceptible to expectancy response, and more consistent with clinical effects (e.g., 4 mg alprazolam severe sedation).

**Conclusions:** Bipolar scales have preferred measurement properties and should be used where possible. Differences from placebo were typically >30% for positive effects and <30% for negative effects while low doses showed 20-30% differences. Stimulants/opioids had steeper, more pronounced dose-response curves than C-IV sedatives. Clinically important differences from placebo are minimally 20-30% for all abused drugs, but dose-response, time course, and maximal effects determine overall abuse potential.

**Support:** Kendle Early Stage, Toronto, Canada.



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### REDEFINING RETENTION: THREE PATHWAYS FOR EXTENDING A TREATMENT EPISODE BEYOND A METHADONE PROGRAM'S BOUNDARIES.

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**Aims:** To expand the definition of treatment retention by illustrating three ways in which methadone patients are retained in treatment after program discharge. **Methods:** Eighteen newly admitted methadone treatment program (MTP) patients received semi-structured interviews at admission and at three follow-up points over 12 months. Of these, six had left their original MTP but were in treatment elsewhere at their final interview. Using a modified grounded theory approach, these six respondents were identified and grouped into one of three mutually exclusive and exhaustive categories based upon the factors associated with the transfer process. An intra-case comparison was then conducted to identify factors contributing to discharge from the original program and entry into the succeeding program.

**Results:** Program transfer was indicative of a patient's commitment to continuing treatment and in five out of the six cases it was accomplished without assistance from the original MTP. The reasons for leaving the original MTP included both voluntary and involuntary circumstances. The sole instance of assisted transfer involved a pregnant patient. Most cases involved moving from one MTP to another with assistance from an outside agency (e.g., needle exchange program) and through the efforts of the participants themselves. Some participants were able to make the transfer without a lapse in treatment but others were unable to enter the succeeding program seamlessly and had to find ways to "maintain" themselves in the community while waiting for the next treatment opportunity.

**Conclusions:** Transfer from an MTP to another program is an important phenomenon and should be viewed as a continuation of treatment rather than a failure in retention. Such transfers may be a positive indicator of a patient's commitment to treatment, and MTP assistance in making the transfer should be both provided and encouraged by the programs whenever possible.

**Support:** NIDA RO1 DA 0158420

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### GENDER DIFFERENCES IN SITUATIONAL ACTIVITIES ASSOCIATED WITH HEROIN AND COCAINE USE AMONG METHADONE-MAINTAINED OUTPATIENTS.

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**Aims:** To examine relationships between situational activities and heroin and cocaine use, and whether they differ by gender.

**Methods:** 114 methadone-maintained (71 male, 43 female), cocaine- and heroin-abusing outpatients provided data regarding their drug use in real time in their daily environments using personal digital assistants (PDAs). Participants were told to initiate an entry each time they craved or used cocaine or heroin; they also responded to random prompts from the PDA to capture base rates of activities. The analyses reported here focus on 15 routine activities. Random-effects logistic-regression models were used.

**Results:** 14,918 person-days of data were collected. Males reported 212 heroin and 414 cocaine-use-events; females reported 80 and 265, respectively. Resting and chores were associated with decreased likelihood of heroin use, arguing was associated with increased likelihood, but these associations did not vary by gender. Thinking was associated with increased heroin use among females (OR=3.2, p=0.05) and not associated with use in males (OR=0.23, p=0.17). Resting, working, chores/hygiene and childcare were all associated with decreased likelihood of cocaine use; listening to music, socializing, arguing, shopping, sports/recreation, thinking, walking, and copping were associated with increased likelihood. Two activities showed directional differences by gender: TV watching was associated with decreased likelihood of cocaine use among females, with a trend toward increased likelihood of cocaine use among males (OR=1.2, p=0.06). Copping was not associated with cocaine use in men (OR=1.7, p=0.18); but it was strongly associated with increased likelihood in women (OR=13.4, p<0.0001).

**Conclusions:** Associations between activities and drug use varied significantly by drug type, as might be expected. However, associations also differed between men and women, emphasizing the value of taking gender into account when individualizing treatment.

**Support:** Research was supported by NIDA-IRP.

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### THERAPEUTIC IMPLICATIONS OF DELTA OPIOID RECEPTOR EXPRESSION IN THE VTA OF ETOH DRINKING OR MORPHINE-INJECTED LEWIS RATS.

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**Aims:** Opioid actions in the ventral tegmental area (VTA) are implicated in the reinforcing effects of ethanol (EtOH). Additionally, the delta opioid receptor (DOR) is neuroprotective following a variety of neural injuries. We have previously shown that VTA microinjection of the DOR agonist DPDPE decreases 2 bottle choice EtOH (10%) consumption in chronically drinking animals and that this effect is greatest in low-drinkers. Furthermore, inhibition of GABA release onto VTA neurons is inversely correlated with amount of ethanol consumed. Conversely, VTA infusion of the DOR selective antagonist TIPP-ψ increases drinking and this effect is blocked by local pretreatment with the GABAA receptor antagonist bicuculline. Here we hypothesized that DOR expression in male Lewis rats would increase rapidly upon initiation of drinking and return to baseline levels following alcohol abstinence.

**Methods:** We used a combination of immunohistochemistry and slice electrophysiology to mark the expression and function of DOR at different time points following EtOH exposure. We also prescreened rats for vulnerability to EtOH consumption using the elevated plus maze and rotarod test.

**Results:** We find that although DOR-IR is sparse in the VTA prior to EtOH consumption, DOR-IR is increased in chronically drinking rats. Importantly, DOR is functional in the VTA following 3, 7, or 14 days of EtOH gavage (30% EtOH daily), regardless of predicted consumption. Additionally, DOR remains functional following 3 days of EtOH abstinence in chronic drinking rats. Administration of low dose morphine (.5 mg/kg sc) similarly induces DOR-IR throughout the VTA, suggesting that multiple drugs of abuse induce DOR expression.

**Conclusions:** These data suggest that the VTA DOR emerges following acute EtOH exposure but that the protective effects of DOR subside in some rats following chronic use. Together with our previous results, these data emphasize the potential therapeutic importance of DOR agonists in treatment of alcohol and opioid abuse.

**Support:** DOD and California State Funds.

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### MOTIVES FOR NON-MEDICAL PRESCRIPTION OPIOID USE AMONG RADARS® SYSTEM COLLEGE SURVEY RESPONDENTS—INDICATION OF A SUBSTANCE ABUSE DISORDER?

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**Aims:** Non-medical prescription (NMRx) opioid use is increasing on American college campuses. However, it is not known whether these users meet substance abuse disorder criteria. Current research suggests that those who use opioids exclusively for pain are less likely to be identified as problematic drug users than those who use opioids for any combination of motives (McCabe, et al., 2007; Zacny, 2008). Self-described motives for NMRx opioid use were compared to DAST-10 scores.

**Methods:** 2000 college students sampled equally from 4 US regions (W, NW, S, NE) completed an online questionnaire in 08/2008 including questions about NMRx opioid use motives (pain, get high, curiosity, study aid, fit in, induce sleep, safer than illicit drugs, treat withdrawal, addict) and a standardized substance abuse screening instrument (DAST-10). Users were classified according to motive for use and DAST-10 scores (0-10).

**Results:** Of 2000 respondents, 231(12%) were NMRx opioid users. Of those, 52(23%) identified pain as the only motive and 179(77%) indicated other motives (motives other than pain relief or pain relief plus other motives). Of those who indicated pain as the only motive, 16(31%) scored >2 on the DAST-10 suggesting problematic drug use. For those indicating other motives for use, 75(42%) scored >2 on the DAST-10 (p=0.15).

**Conclusions:** The data do not support a difference between those who use NMRx opioids exclusively for pain and those who use for other motives (power is 69%, using the 11% observed difference between groups in number of abusers). However, a surprising number of NMRx opioid users who indicated pain as their only motive for NMRx use received a DAST-10 score suggesting problematic drug use. Therefore, providers should consider these data when prescribing pain medication for college students.

**Support:** Denver Health is a public non-profit organization providing data to industry, regulatory agencies and researchers through the RADARS System.



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**WAKING AT NIGHT TO SMOKE IN ADOLESCENT AND ADULT SMOKERS.**

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**Aims:** Recently smokers who rise at night to smoke (NTS) have become a focus of research, but no studies have described NTS in adolescent smokers. The goal of this presentation is to better characterize NTS across the lifespan.

**Methods:** We used a data set (N = 573) pooled from five previously completed studies involving smoking cessation, smoking reduction, or cross-sectional description. Each study generally used identical measures in the baseline phase. Unlike earlier reports, we had available a sample of adolescent smokers (n = 118), providing an overall age range from 13-79 years-old.

**Results:** Twenty-three percent of individuals reported NTS. Multivariate logistic regression analysis revealed both linear ( $p < 0.01$ , OR = 0.60, 95%CI = 0.45,0.80) and quadratic ( $p < 0.01$ , OR = 1.002, 95%CI = 1.002,1.0003) effects of age. Peak rates of NTS were observed in the teenage years followed a decline in the twenties and then relatively stable rates across the lifespan. In addition, those rising at night to smoke were more likely to smoke within 5 minutes of waking in the morning ( $p < 0.01$ , OR = 3.58, 95%CI = 1.95,6.56), to smoke medium or regular filter cigarettes ( $p < 0.01$ , OR = 2.24, 95%CI = 1.30,3.85), to have become regular smokers at a younger age, ( $p < 0.05$ , OR = 0.90, 95%CI = 0.83,0.98), and to be heavier smokers, ( $p < 0.05$ , OR = 1.04, 95%CI = 1.01,1.07). In addition, relative to Whites, African Americans ( $p < 0.05$ , OR = 5.05, 95%CI = 1.40,18.17) and Hispanics ( $p < 0.05$ , OR = 3.56, 95%CI = 1.32,9.63) were more likely to be night smokers.

**Conclusions:** Our study revealed novel differences in NTS by age of smoker and race, as well as replicating earlier findings that NTS is associated with indices of greater nicotine dependence. However, the cross-sectional nature of our design requires replication in a longitudinal framework to confirm trends in NTS across the lifespan.

**Support:** This research was supported by the NIDA grant P50-DA13333. Dr. Mooney is supported by a NIDA Career Development award K01-DA-019446.

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**MEDICAL OUTCOMES IN METHAMPHETAMINE-DEPENDENT ADULTS 3 YEARS AFTER TREATMENT.**

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**Aims:** Medical conditions in methamphetamine (MA) users have not been well characterized. Using both self-report and physical examination data, the aims of this study were to: (1) describe the frequency of medical conditions in a sample of MA users three years post-treatment; (2) evaluate the association between medical conditions and MA use frequency; and (3) examine the relationship of route of administration with medical outcomes.

**Methods:** MA dependent adults (N=301) who participated in the Methamphetamine Treatment Project (MTP) were interviewed and examined 3 years after treatment. Medical, demographic and substance use characteristics were assessed using the Addiction Severity Index and Life Experiences Timeline. Current and lifetime medical conditions, ECG characteristics, and physical exam abnormalities were assessed.

**Results:** Among the most frequently reported lifetime conditions were wounds and burns (40.5%, N=122) and dental problems (33%, N=99), and a significant proportion of the sample evidenced prolonged QTc interval (19.6%, N=43). Although health conditions were not associated with frequency of MA use during follow-up, intravenous MA use was significantly associated with missing teeth (OR=2.4, 95% C.I., 1.2-4.7) and hepatitis C antibodies (OR=13.1, C.I., 5.6-30.1).

**Conclusions:** In this sample of MA users, dental problems and QTc prolongation were observed at elevated rates. Although post-treatment MA use frequency was not associated with a majority of medical outcomes, intravenous MA use exacerbated risk for dental pathology and hepatitis C. Longer-term follow-up research is needed to elucidate health trajectories of MA users.

**Support:** This research was supported 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 Health and Human Services.

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**GENDER DIFFERENCES IN CRIMINAL RATIONALIZATION AMONG PRISON-BASED SUBSTANCE ABUSE TREATMENT PARTICIPANTS NEARING COMMUNITY RE-ENTRY.**

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**Aims:** Many substance abuse treatment programs include cognitive restructuring components targeting “criminal thinking” as a method of preventing relapse or recidivism. The purpose of this research is to examine gender differences among factors associated with criminal rationalization (CR), or the extent to which offenders justify or neutralize their deviant thinking and/or behaviors.

**Methods:** Participants were recruited as part of the CJDATS multi-site trial, “Transitional Case Management.” 490 male and 147 female participants who identified as either white or African American were selected for this analysis. Linear regression was used to determine factors associated with CR, which was measured by a composite score of eight items from the Texas Christian University Client Evaluation of Self at Intake (CESI) (Range: 8-40). The mean age was 34.7 years. Most participants did not complete high school (64.4%) and were not married (83.3%).

**Results:** Participants most commonly reported alcohol (53.7%), marijuana (41.3%), methamphetamine (30.8%), and crack (25.9%) as drugs used weekly in the year prior to incarceration. Being of an African American ethnicity (B=2.96, SE=.61,  $p < .001$ ), higher levels of marijuana use (B=1.62, SE=.56,  $p < .005$ ), and lower levels of methamphetamine use (B=-1.33, SE=.66,  $p < .05$ ) in the year prior to prison were factors significantly associated with higher levels of CR among men. For women, being older (B=.148, SE=.07,  $p < .04$ ), higher levels of methamphetamine use (B=2.56, SE=1.24,  $p < .04$ ), and having fewer probation or parole violations (B=-1.73, SE=.63,  $p < .01$ ) were associated with higher levels of CR.

**Conclusions:** Results indicate that there are gender differences in CR among prison-based treatment participants. Interestingly, methamphetamine use was negatively associated with CR for men but positively associated with CR for women. This finding supports the need to target cognitive differences between male and female offenders in substance abuse treatment programs.

**Support:** This research was supported by the National Institute on Drug Abuse (U01-DA016205).

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**DEVELOPING SCIENCE-BASED TREATMENT FOR OPIOID-DEPENDENT YOUTH: LESSONS LEARNED.**

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**Aims:** We have been conducting clinical trials research focused on developing and evaluating science-based treatment for opioid-dependent youth. As evidence-based treatment is not routinely provided in clinical settings for this population, disseminating information on acceptability as well as efficacy outcomes is essential.

**Methods:** We report on our systematic evaluation of our current treatment protocol, as well as a case study evaluation of treatment completers, to describe structural and individual-level characteristics associated with retention among a group of opioid-dependent adolescents and young adults participating in a clinical trial comparing the relative effectiveness of a shorter (28-day) or longer (63-day) detoxification with buprenorphine.

**Results:** Since the trial's inception, we have identified several structural issues which promote greater recruitment and retention, including twice weekly attendance (as opposed to more frequent attendance requirements); inclusion of 13-18 as well as 19-24 year olds; ensuring a sufficient range of starting dosing of buprenorphine (6-16 mg); allowing flexibility in appointment times; opening an additional study site to ensure treatment is in closer proximity to the target population; and expanding recruitment strategies to include street outreach. Of youth enrolled in this trial, (n=44; 63% Male; Mean Age = 20; SD = 2.73), treatment completion appears to be associated with dependence on opioids and few, if any, other drugs; at least 1 previous treatment experience; few diagnosed psychiatric co-morbidities other than depression; and opioid-negative urine results throughout treatment.

**Conclusions:** These novel data on this understudied group may help to inform future treatment efforts. Results indicate that a lower threshold to accessing treatment and specific individual-level characteristics may facilitate recruitment and retention.

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### SYSTEMATIC REVIEW OF COMPUTER-BASED TREATMENTS FOR DRUG ABUSE AND DEPENDENCE.

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**Aims:** To conduct a systematic review of clinical trials of computer-based treatments for drug abuse and dependence. A range of innovative computer-based interventions for psychiatric disorders have recently been developed and shown to be effective. Computer-based interventions for drug abuse are promising due to reduced cost and greater availability compared to traditional treatment.

**Methods:** Electronic searches were conducted using MEDLINE, Psychlit, and EMBASE identifying English language studies of human participants from 1966 to November 19, 2008. CPDD abstracts from 2003-2007 were also hand searched. 400 non-duplicate records were identified. Two reviewers classified abstracts for study inclusion ( $\kappa = .76$ ). 388 articles were excluded: 96 were not research studies, 157 did not include a computer-based intervention of patients, 25 were not for substance related disorders, 60 were for tobacco disorders, and 50 were for alcohol disorders. Two reviewers independently determined quality index scores based on a 31-point scale by Downs and Black assessing internal and external validity (inter-rater reliability = .87).

**Results:** Study quality was moderate ( $M = 15.8$ ,  $SD = 5.2$ , range = 6 - 24). Across studies, interventions showed high patient acceptability despite substantial variation in type and amount of treatment ranging from brief, single-session motivational enhancement to multi-session, highly-interactive interventions. 9 articles were pilot or full-scale trials of a computer-based treatment compared to a control condition, although only 3 articles reported substance-use outcomes. Compared to treatment-as-usual, participants in computer-based treatment conditions showed higher motivation to change, better retention, greater knowledge of presented information, and less substance use.

**Conclusions:** High patient acceptability, improved retention and initial indications of efficacy suggest that computer-based treatments are highly promising. Methods of extending treatment access and providing intervention in real-world settings should be explored.

**Support:** NIDA grant K01-DA022398

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### OVARIAN HORMONES AND SUBJECTIVE RESPONDING TO STRESS AND CUES IN COCAINE-DEPENDENT FEMALES.

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**Aims:** Ovarian hormones (estradiol and progesterone) have a significant impact on drug craving, and may account for the well established gender differences in substance-dependent individuals. For example, cocaine-dependent females appear to be more susceptible to stress induced craving and relapse than cocaine-dependent males. However, most of the data in clinical samples has focused on the impact of sex steroids on the response to the drug itself, and little is known about the role that ovarian hormones play in subjective response to cues and stress. Therefore, the goal of the present study was to determine the impact of ovarian hormones on craving and stress in response to cues (drug paraphernalia), corticotropin releasing hormone (CRH), and the Trier Social Stress Task (TSST).

**Methods:** Groups of cocaine-dependent females ( $n=20$ ) and control females ( $n=24$ ) were admitted for a two-day hospital stay at MUSC. Each subject received an i.v. infusion of CRH (1 ug/kg), participated in the TSST, and completed a cue-reactivity session. Peak responding was assessed by measuring percent change ( $100 * (\text{maximum-baseline})/\text{baseline}$ ) in subjective ratings of stress and craving. Plasma samples were collected prior to the tasks and the progesterone and estrogen levels were quantified by radioimmunoassay.

**Results:** CRH administration in cocaine-dependent females produced a significant positive correlation (Spearman's rank correlation coefficient) between progesterone and stress ( $r_s=0.483$ ;  $p<0.05$ ), progesterone and craving ( $r_s=0.453$ ;  $p=0.05$ ), and a trend towards a significant correlation between estradiol and stress ( $r_s=0.647$ ;  $p=0.06$ ). No other significant correlations were observed between ovarian hormones and subjective stress and craving in response to the cue or the TSST tasks.

**Conclusions:** These data suggests that the CRH systems that mediate stress and craving in cocaine-dependent females are sensitive to circulating ovarian hormones.

**Support:** (NIH-NIDA & ORWH;P50 DA016511) (NIH-NCRR; M01 RR01070)

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### GENERALITY OF DISRUPTION OF PREPULSE INHIBITION BY THE DOPAMINE AGONIST APOMORPHINE.

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**Aims:** Sensorimotor gating, the process by which organisms filter extraneous sensory stimuli, is commonly assessed with manipulations of prepulse inhibition (PPI). Alterations in gating are observed in individuals with schizophrenia, HIV-1 dementia and other neuropsychiatric disorders. Dopaminergic pathways play a putative role in sensorimotor gating. It is well-established that apomorphine, a dopamine agonist, disrupts PPI of the auditory startle response at low prepulse intensities (75 dB) at an interstimulus interval (ISI, time between the prepulse and the startle stimulus) of 100msec. In the present study, it was hypothesized that disruption of PPI by apomorphine would also occur with a tactile prepulse stimulus, and further, that a range of ISIs would provide a more precise index of any such disruption. It was also hypothesized that PPI of the auditory startle response would be disrupted by apomorphine with a prepulse of a higher intensity (85 dB), when assessed with a range of ISIs.

**Methods:** Accordingly, sensorimotor gating was measured with tactile and auditory prepulse stimuli in the PPI paradigm (ISIs of 0, 8, 40, 80, 120, 4000 msec, 6 trial blocks, Latin square design). A within-subjects design was used for each experiment, with 12 adult male Sprague-Dawley rats that were tested 5 minutes after a subcutaneous injection of saline or one of three apomorphine (APO) doses (0.1, 0.25, and 0.5 mg/kg) in an ascending series with 48 hr between assessments.

**Results:** Tactile PPI was disrupted as a linear function of apomorphine dose at the 40 msec ISI. At the 100 msec ISI, although there was disruption of PPI at all doses, there was no dose-response effect. Auditory PPI with a prepulse intensity of 85 dB was not significantly disrupted by apomorphine at the 100 msec ISI, as found previously. However, there was a leftward shift of the ISI function with dose of APO.

**Conclusions:** These results indicate the generality of PPI disruption by apomorphine across prepulse stimulus modalities and the importance of manipulating the temporal dimension of PPI instead of using a single ISI.

**Support:** DA13137, HD043680

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### AN INTEGRATED INTERVENTION FOR CHRONIC PAIN AND SUBSTANCE USE REDUCES OPIOID MEDICATION MISUSE.

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**Aims:** To examine the effectiveness of a brief integrated intervention for chronic pain in veterans with comorbid substance use disorder (SUD).

**Methods:** Patients were referred by their primary care providers if they had chronic pain and comorbid SUD. The intervention consisted of an assessment and development of treatment recommendations by a team including an addiction psychiatrist and an anesthesia pain specialist. Recommendations often included assistance with detoxification or change to long-acting opioids with ongoing monitoring. Retrospective chart review was used to evaluate changes in indicators of misuse of opioid medications and utilization of medications and healthcare services 12 months pre-intervention and 12 months post-intervention.

**Results:** Complete data are available for 47 participants. The average age was 50 years ( $SD=7.7$ ), 93% were male, and 54% were married. The most common pain diagnoses were back pain (90%), neck or joint pain (88%), or rheumatoid arthritis or osteoporosis (85%). SUDs included alcohol (61%), opioid (39%), cannabis (29%), amphetamine (15%), or other SUD (42%). In the 12 months post-intervention, there were reductions in the proportions of several indicators of opioid misuse compared to the 12 months pre-intervention, including reports of lost/stolen medication (15% pre- versus 11% post-treatment), using opioids for purposes other than pain control or over-use of pain medications (38% versus 21%), and concurrent use of alcohol or illicit substances while taking an opioid (60% versus 32%). There were no significant differences in pre- versus post-intervention rates of appointment utilization, emergency room visits, mental health visits, substance abuse treatment visits, participation in physical therapy, or use of pain medications.

**Conclusions:** Participation in an integrated pain and SUD consultation clinic is associated with significant reductions in indicators of misuse of opioid medications. The one-time session was not associated with changes in medical utilization.

**Support:** The authors have no financial relationships that related to the topic of this presentation.

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### COMPARISON OF THE PHARMACOLOGY OF METHYLENEDIOXYAMPHETAMINE AND 3,4-METHYLENEDIOXYMETHAMPHETAMINE CONSUMED IN A RECREATIONAL SETTING.

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**Aims:** Analyses of illicitly sourced ecstasy pills typically find the primary active agent to be 3,4-methylenedioxyamphetamines (MDMA); less commonly, 3,4-methylenedioxyamphetamine (MDA) or a mixture of these ring-substituted amphetamines is found. Both drugs are psychoactive and the aim of this study was to compare their effects in a "naturalistic" setting.

**Methods:** As part of a larger study designed to investigate the clinical pharmacodynamic and pharmacokinetic profile of illicitly sourced ecstasy in recreational settings, physiological and pharmacological measures were gathered at parties from 56 ecstasy users. Samples of the pills consumed were also analysed for content. Seven participants (3 males and 4 females) consumed MDA rather than MDMA. This subset was compared with 7 matched users who had consumed MDMA. Pharmacodynamic effects including heart rate and blood pressure were measured. Blood was taken from participants both before ecstasy consumption and hourly thereafter and analysed for plasma drug concentrations. All subjects were genotyped to identify variations in the CYP2D6 metabolism.

**Results:** Initial analyses indicate that subjects consumed between 11 and 80mg of MDA, and maximum MDA plasma concentrations ranged from 89 to 240 ng/mL. All subjects were CYP2D6 extensive metabolisers. MDA users showed significant increases in heart rates of 20 bpm ( $p < 0.05$ ), and systolic blood pressure of 16 mm Hg ( $p < 0.05$ ). Comparisons of the effects of the two drugs on subjective, other physiological and endocrine effects will also be presented.

**Conclusions:** Initial analyses of these data suggest little difference in effects between users that ingested MDA and those ingesting MDMA.

**Support:** National Health and Medical Research Council of Australia to RJ Irvine & JM White.

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### EFFECTS OF (-)-TRANS-PAT, A NOVEL 5-HT<sub>2C</sub> AGONIST AND 5-HT<sub>2A/2B</sub> ANTAGONIST/INVERSE AGONIST, ON AMPHETAMINE-INDUCED LOCOMOTOR ACTIVITY IN RATS.

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**Aims:** Serotonin (5-HT) 2A and 2C receptors are widely expressed in the central nervous system, and drugs interacting with these receptors are known to modulate dopamine neurochemistry and the behavioral effects of dopaminergic compounds. There is an increasing interest in developing potential therapeutic compounds targeting these receptor systems for psychiatric disorders such as depression, schizophrenia, compulsive eating, and drug addiction. (1R,3S)-(-)-trans-1-phenyl-3-dimethylamino-1,2,3,4-tetrahydronaphthalene (PAT) is a novel compound that functions as a high-efficacy agonist at 5-HT<sub>2C</sub> receptors and an inverse agonist at both 5-HT<sub>2A</sub> and 5-HT<sub>2B</sub> receptor subtypes. (-)-trans-PAT has approximately 10-fold and 300-fold higher affinity for 5-HT<sub>2C</sub> relative to 5-HT<sub>2A</sub> and 5-HT<sub>2B</sub> receptors, respectively. The primary goal of this study was to examine the effects of (-)-trans-PAT administration on the locomotor-activating effects of d-amphetamine in rats.

**Methods:** Male, Sprague-Dawley rats were tested (up to two times per week) in standard activity chambers (Med Associates, Inc.) to assess locomotion during 1-hour sessions. (-)-trans-PAT (3 – 30 mg/kg, i.p.), d-amphetamine (0.5 – 2 mg/kg, i.p.), and saline (i.p.) were administered immediately before the session and tested alone and in combination.

**Results:** d-amphetamine resulted in dose-dependent increases in locomotion (ED<sub>50</sub> value, ~1.0 mg/kg) that were sustained across the one-hour session. (-)-trans-PAT (ED<sub>50</sub> value, ~10 mg/kg) produced a dose-dependent attenuation of d-amphetamine-stimulated locomotion that was more pronounced in the 2nd half of the session.

**Conclusions:** These are the first data obtained in rats examining this novel 5-HT<sub>2C</sub> agonist/5-HT<sub>2A</sub> inverse agonist, and demonstrate its effectiveness in attenuating amphetamine's behavioral effects.

**Support:** Supported by NIH R01DA023938

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### EFFECTS OF MODAFINIL ON SLEEP ARCHITECTURE IN CHRONIC COCAINE USERS.

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**Aims:** To determine the effect of morning-dosed modafinil on sleep architecture and daytime sleepiness in chronic cocaine users

**Methods:** 18 chronic cocaine users were studied in a placebo-controlled, double-blind, randomized trial of modafinil in an inpatient setting. Participants were randomized to receive modafinil 400mg or placebo every morning at 7:30am for 16 days. Participants underwent polysomnographic sleep recording on days 1-3, 7-9 and 14-16 (1st, 2nd and 3rd weeks of abstinence). Multiple sleep latency tests (MSLT) were given at 11:30am, 2pm, and 4:30pm on days 2, 8, and 15. Subjective sleep quality and alertness were measured daily.

**Results:** Modafinil was associated with decreased nighttime sleep latency and increased slow-wave sleep time. Modafinil interacted with abstinence week and was associated with longer sleep times in the 2nd and 3rd week of abstinence and shorter latency to REM sleep in the 3rd week of abstinence. Modafinil was associated with increased latency to daytime sleep measured by the MSLT and a trend toward decreased subjective daytime sleepiness.

**Conclusions:** Modafinil improves sleep architecture in abstinent cocaine users and decreases daytime sleepiness.

**Support:** 1KL2RR024138; DA011744-06

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### ASSOCIATED FACTORS OF NON-USE OF DRUGS AMONG CHILDREN AND YOUTH IN STREET CIRCUMSTANCES IN BRAZIL.

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**Aims:** Verify associated factors of non-use of drugs among children and youth in street circumstances in Brazil.

**Methods:** A national cross sectional survey were developed in 93 welfare services for street youth in 27 Brazilian states capitals. 10 to 18-years-old in street circumstances were interviewed using a WHO questionnaire to non-student youth. Data regarding substance use, demographic characteristics, school status, family bonding, time spent on the streets and out-of-home history and domestic violence were assessed. Results were compared through chi-square test with level of significance of 1% among the group of those who used drugs and those who did not use (including alcohol and tobacco).

**Results:** Among the 2802 respondents, 493 had never engaged in substance use. 83.6% of non-users attended school against 49.9% of users. Family bonding was also associated with non engagement in substance use (95.9% of non-users vs 63.1% of users). Domestic violence was referred by 36.3% of non-users and 58.8% of users. Out-of-home history of less than one year was associated to non-engagement in substance use (49.7% in non-users vs 26.3% in users). Non users (62.4%) spent less time on the streets in comparison to 35.9% of user that spent a maximum 5 hours on the streets. Although knowingly males are more subject to drug use, in this population, we found an equal distribution among males and females, thus gender was not a decisive factor. Since age appears a principal risk factor known, after analyzing the same variables mentioned before stratified by ages, the results kept statistically significant difference for all the variables in each stratum.

**Conclusions:** Family bonding, school attendance, lack of domestic violence and lesser exposure to street environment are aspects associated to non-engagement in substance use by children and youth in street circumstance in 27 Brazilian state capitals.

**Support:** SENAD and AFIP

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### THE REINFORCING EFFICACY OF 3 VS 6 PUFFS IN SMOKERS: COMPARING TRADITIONAL AND DEMAND ANALYSIS.

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**Aims:** Demand curve analysis has been demonstrated to characterize the results of the three traditional laboratory abuse potential assessment methods – peak maintained response rate, progressive ratio break point, and preference in situations of choice – better than does the concept of relative reinforcing efficacy (RRE) when qualitatively different reinforcing commodities were tested. The 2 characterizations are predicted to be identical when the reinforcers are qualitatively the same, but different in magnitude. Here we test this prediction.

**Methods:** Ten nicotine deprived cigarette smokers earned standardized puffs by pulling response plungers on reinforcement schedules that increased the response requirement across sessions. In 2 phases, 3-puff and 6-puff magnitude reinforcers were independently (sequentially) assessed for their reinforcing potency; and in phase 3, they were assessed concurrently (a choice arrangement). Total puffs, breakpoints, peak response output, and preference measures were calculated.

**Results:** Across independent conditions, mean total puffs consumed was significantly higher ( $p = .002$ ) in the 6-puffs condition compared to the 3-puffs condition; median breakpoints for the two reinforcers were identical ( $p = .31$ ); and median peak response rates were significantly higher ( $p = .04$ ) in the 6-puff condition. In the concurrent choice condition, responding occurred almost exclusively on the 6-puff plunger. Break point and peak maintained response rate measures were strongly and positively correlated with the demand-curve measures Pmax (Spearman's  $r = 0.97$ ,  $p < 0.0001$ ) and Omax (Pearson's  $r = 0.99$ ,  $p < 0.0003$ ), respectively. Preference for the concurrent 6-puff reinforcer was predicted by the 6-puff demand curve being higher than the 3-puff demand curve at all response requirements.

**Conclusions:** For qualitatively similar reinforcers – unlike for some other classes of reinforcers – the RRE concept accounts for the results observed from the 3 traditional measures of reinforcing potency as well as does demand curve analysis.

**Support:** NIDA Grant R37 DA6526

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### EFFECTS OF AMPHETAMINE DERIVATIVES ON MEMORY PERFORMANCE AND TISSUE CONTENT OF MONOAMINE AND AMINO ACID NEUROTRANSMITTERS IN MICE.

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**Aims:** Structural derivatives of amphetamine are some of the most commonly abused drugs. Considerable evidence has shown that certain amphetamine derivatives deplete brain levels of monoamine neurotransmitters. For example, methamphetamine exposure can lead to persistent reductions in dopamine concentration. However, relatively little work has examined whether this effect extends to amino acid neurotransmitter systems. Furthermore, the functional consequences of amphetamine derivative induced neurochemical depletion remain to be convincingly demonstrated. In this study, mice were non-continuously exposed to dosing regimens of methamphetamine, methylenedioxymethamphetamine (MDMA), or para-chloroamphetamine (PCA), known to deplete monoamines.

**Methods:** Long-term and short-term memory performance was assessed by measuring behavior in a passive avoidance and a delayed match to position assay, respectively. Tissue content of monoamines was determined ex vivo using high pressure liquid chromatography whereas tissue content of glutamate and GABA was assessed ex vivo via proton magnetic resonance spectroscopy.

**Results:** Consistent with previous studies, significant reductions in tissue content of monoamines were readily apparent. Furthermore, changes in amino acid neurotransmitters were also evident. Finally, deficits in long-term memory performance were only demonstrated in animals exposed to PCA whereas short-term memory performance was more susceptible to disruption through exposure to MDMA.

**Conclusions:** These studies demonstrate that the neurochemical effects of amphetamine derivatives in mice extend beyond monoaminergic systems and provide evidence that memory performance can be impaired by exposure to these compounds.

**Support:** Support provided by USPHS grants (DA 00517, RR 00165, DA 020645, RR 020146, and DA 024760).

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### SEX DIFFERENCES IN THE INTERACTIONS BETWEEN SOCIAL RANK AND COCAINE REINFORCEMENT IN CYNOMOLGUS MONKEYS.

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**Aims:** Earlier work in male cynomolgus monkeys showed that dopamine D2 receptor availability, as measured with positron emission tomography (PET), and cocaine reinforcement were influenced by social rank (Morgan et al., *Nature Neurosci* 5: 169, 2002). The present study extended this work to female cynomolgus monkeys and to acquisition and maintenance of cocaine self-administration.

**Methods:** Baseline PET measures of D2 receptor availability using [18F]fluorocleobopride were obtained in individually housed monkeys and again after 3 months of social housing. Following completion of these measures, monkeys self-administered cocaine (0.001-0.03 mg/kg/inj) under a fixed-ratio 30 schedule.

**Results:** D2 receptor availability did not predict eventual social rank. After 3 months of social housing, D2 receptor availability significantly increased in monkeys that became dominant, an effect similar to that reported in male monkeys. However, unlike in males, cocaine acquisition (defined as the lowest dose of cocaine that functioned as a reinforcer) occurred at lower doses and the peak of the cocaine dose-response curve was higher in dominant compared to subordinate monkeys.

**Conclusions:** These findings suggest that the relationship between social rank and dopamine receptor function is similar in males and females, but the consequence of elevated D2 receptor availability on cocaine reinforcement is fundamentally different according to the sex of the animal. It remains possible that the elevated D2 receptor availability in males and females occurred via different mechanisms (i.e., elevated D2 receptor densities or decreases in extracellular dopamine). In addition, the social interactions in same-sex groups are fundamentally different in males and females which may account for the sex differences observed. These findings highlight the importance of studying social variables in drug abuse and the likely sex differences involved in these interactions.

**Support:** DA17763, DA10584.

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### NEUROPSYCHOLOGICAL TEST PERFORMANCE IN CURRENT AND ABSTINENT METHAMPHETAMINE USERS.

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**Aims:** This study aims to evaluate the cognitive function of both current and abstinent METH-users compared to non-drug-user controls.

**Methods:** Current METH-users (< 4 days since last use), abstinent (28days-24mos) METH-users, and controls ages 18-57 were enrolled. The neuropsychological test (NPT) battery assessed 5 cognitive domains: visual and verbal memory, attention, working memory, fluency, motor; and overall global score.

**Results:** 26 current METH-users, 33 abstinent METH-users, and 32 non-drug-user controls who were well-matched by age and education, completed their NPTs. Current METH-users performed the worst on all domains of the NPTs compared to abstinent METH-users and controls. There were significant differences between the groups in the NPT domains of motor (ANOVA  $p=0.04$ ) and global scores (ANOVA  $p=0.048$ ). Current METH-users performed significantly lower on the NPT motor domain compared to controls ( $p=0.02$ ) and abstinent METH-users ( $p=0.03$ ). Current METH-users also performed significantly lower on the global scores ( $p=0.02$ ) compared to abstinent METH-users, and a trend toward significance ( $p=0.06$ ) when compared to controls.

**Conclusions:** Our findings of lower NPT scores in METH-users, especially the current-users, suggest that METH use might lead to cognitive deficits. A larger sample size is needed to validate these preliminary findings. Longitudinal follow-up may help to determine whether some of these cognitive deficits normalize with prolonged abstinence.

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### EFFECT OF INDIVIDUAL VS DYADIC RELAPSE PREVENTION ON STRESS LEVELS OF CAREGIVERS OF ALCOHOL-DEPENDENT SUBJECTS: CORRELATES OF CAREGIVER STRESS.

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**Aims:** Compare Individual/Dyadic Relapse Prevention on stress levels of caregivers of alcohol dependent subjects; explore correlates of caregiver stress

**Methods:** Study was carried out at NIMHANS, India. Participants were caregivers of 60 alcohol dependent inpatients, randomized to Individual Relapse Prevention (IRP) and Dyadic Relapse Prevention (DRP), with 30 subjects in each group. Intervention was a Relapse Prevention Module developed for the study and administered over 3 weeks; average number of sessions was 10 for each patient/dyad (caregivers stayed with their respective subjects on the unit). In IRP, intervention was administered to the individual patient; in DRP, intervention was administered to patient and his caregiver (Dyad). Caregiver stress was measured by Perceived Stress Scale (Sheldon Cohen, 1983)

**Results:** (a) At 3-months following discharge of the subjects, stress scores of DRP caregivers were lower, compared to IRP caregivers (mean stress score 8 versus 20\*) (b) Higher the quantity-frequency of alcohol consumption in their respective subjects at 1- and 3-month assessments, greater the caregiver stress (c) Caregiver stress was greater with higher number of days with problems in their subjects in the areas of drinking dyscontrol, family, occupation, ill-health, and neuropsychiatric complaints (d) Baseline stress scores of caregivers were higher if the caregivers were from lower socioeconomic status, were unemployed, and if they were spouses (versus other relatives) of their respective subjects

**Conclusions:** Findings suggest that involving caregivers in treatment (DRP) reduced their stress levels, compared to individual intervention (IRP). The study is novel as it entailed caregiver participation for alcohol dependence treatment for the first time in an Indian population, and also emphasized benefits of participation for the caregivers themselves (as opposed to benefits for the subjects).

**Support:** Work on writing this abstract was supported by the Fogarty Grant (Grant No. TW05811-08)

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### MU/DELTA OPIOID AGONIST INTERACTIONS IN AN ASSAY OF CAPSAICIN-INDUCED THERMAL ALLODYNIA IN RHESUS MONKEYS.

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**Aims:** Mixtures of delta and mu opioid receptor agonists produce synergistic antinociception in models of acute thermal pain in rhesus monkeys. The present study evaluated interactions between delta and mu agonists in an assay of capsaicin-induced thermal allodynia, an assay that models features of inflammatory pain.

**Methods:** Three rhesus monkeys were seated in primate restraint chairs and treated IM with vehicle, the mu agonist methadone (0.32-3.2 mg/kg), the delta agonist SNC80 (1-5.6 mg/kg) or a 0.1:1 mixture of SNC80+methadone (0.01:0.1 - 0.1:1.0 mg/kg). Fifteen min after injections, each monkey's shaved tail was exposed for 5 min to a patch saturated with a capsaicin solution. Tail-withdrawal latencies from water heated to 38, 42 and/or 46°C water were determined before drug treatment and 15, 30, 45 and 60 min after removal of the capsaicin patch.

**Results:** Capsaicin produced transient allodynia, manifested as decreased tail-withdrawal latencies from water heated to a threshold temperature individually determined in each monkey. Methadone or SNC80 alone produced dose dependent anti-allodynia. In addition, the highest dose of methadone produced sedation in all monkeys, and the highest dose of SNC80 produced convulsions in one of three monkey. The 0.1:1 mixture of SNC80/methadone also produced dose-dependent anti-allodynia. ED50 values for methadone and SNC80 in the mixture were lower than ED50 values for methadone or SNC80 administered alone. In addition, full anti-allodynia was produced by a dose of mixture that produced minimal sedation and no convulsions, suggesting that effective doses of the mixture produced fewer undesirable effects than effective doses of methadone or SNC80 alone.

**Conclusions:** Our results are consistent with the hypothesis that combined activation of delta and mu opioid receptors may produce effective analgesia with fewer side effects than selective activation of delta or mu opioid receptors alone.

**Support:** Supported by R01-DA11460 and Intramural Research Programs of NIDA and NIAAA.

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### TIMES, ORGANIZATIONS, OFFICES, LIVES AND SYSTEMS EVOLUTION PROJECT.

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**Aims:** Los Angeles Metropolitan Churches (LAM) and Friends Research Institute (FRI) propose, over the course of 3 years, to develop culturally competent health systems program area to engage in systems change activities and organizational capacity building in South Los Angeles. This proposal will accomplish two primary goals: 1) develop culturally competent guidelines to improve health services for African American populations seeking health services in LA County and 2) conduct organizational capacity development activities for African American community organizations and the individual leaders of these organizations to sustain culturally competent programs in target areas.

**Methods:** The goal of the LAM/FRI TOOLS of Change (Times, Organizations, Offices, Lives and Systems) is to hire necessary health, cultural competence and systems change expertise, and engage 10 AAAOD Executive Directors in a process to develop program guidelines and capacity building for culturally competent system change and engage African American males and their families in services in South Los Angeles.

**Results:** Project will examine access to care, stigmas and service utilization issues. Project activities will inform clarification of policy barriers, administrative challenges, organizational capacity building activities and systems shifts needed to address substance abuse health care services and increase service utilization by African American males.

**Conclusions:** Success of the process and system change elements will be demonstrated by systematic integration of the model in AAAOD's membership and adoption and approval by Los Angeles County's Office of Alcohol and Drug Program Administration. We have to examine bias, stereotyping, prejudice and clinical uncertainty on the part of health providers that may contribute to racial and ethnic disparities in substance abuse treatment for African American men in LA County. These issues are lightning rods in their own right and can invoke resistance among the very organizations we are trying to impact.

**Support:** The California Endowment funds this project.

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### LOBELINE POTENTIATES THE METHAMPHETAMINE-INDUCED DECREASE IN EXTRACELLULAR DOPAC IN THE NUCLEUS ACCUMBENS SHELL.

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**Aims:** Lobeline, an alkaloid found in lobelia inflata, has been shown to decrease methamphetamine self-administration in rats. Recently, lobeline has also been shown to attenuate the acquisition, but not the expression, of methamphetamine conditioned place preference (CPP). It is well established that dopaminergic neurotransmission in the nucleus accumbens shell is involved in mediating the rewarding effects of psychostimulants. The aim of the current study was to determine if lobeline alters methamphetamine-induced dopaminergic alterations in the nucleus accumbens shell.

**Methods:** Microdialysis with HPLC/EC analysis was used to determine if lobeline (0, 1 or 3 mg/kg, SC) alters methamphetamine (0 or 0.5 mg/kg, IP)-evoked alterations in extracellular dopamine or its metabolite dihydroxyphenylacetic acid (DOPAC) in the nucleus accumbens shell of awake, male Sprague Dawley rats.

**Results:** Results indicate that lobeline (1 and 3 mg/kg, SC) alone increased extracellular DOPAC, while having no effect on extracellular dopamine. In contrast, methamphetamine (0.5 mg/kg, IP) alone decreased extracellular DOPAC, while also increasing dopamine; the increase in dopamine was not altered significantly by lobeline. Interestingly, lobeline dose-dependently potentiated the methamphetamine-induced decrease in extracellular DOPAC. Previous work has shown that methamphetamine releases DA into the cytosol by interacting with the vesicular monoamine transporter (VMAT2) and by inhibiting MAO to decrease DOPAC.

**Conclusions:** The current results suggest that lobeline competes with methamphetamine at VMAT2, thus reducing the methamphetamine-induced increase in cytosolic DA available for metabolism by MAO. These results provide further evidence that lobeline has a unique pharmacological profile at VMAT2, thus warranting further investigation in the ongoing development of effective pharmacotherapies for methamphetamine abuse.

**Support:** Research supported by USPHS grant DA17548 to LPD.

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**INHALANT DRUG USE AMONG ISRAELI YOUTH.**

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**Aims:** The use of inhalants is an overlooked global public health problem associated with subsequent illicit drug use, social dysfunction, mental and physical morbidity, and death. We analyzed data from the most recent national high-school survey to describe the epidemiology of inhalant use among Israeli youth.

**Methods:** The study population comprised a nationally representative sample of Jewish and Arab students in grades 7-12. Data was collected in 2005 via an anonymous, self-administered questionnaire. Analyses were performed on 8,631 students.

**Results:** Lifetime, past-year and past-month prevalence rates were 23%, 14%, and 8%, respectively - considerably more prevalent than illicit drugs. Past-month inhalant use prevalence was higher among youth with drug-using friends (Adjusted Odds Ratio=2.2;95%CI=1.8-2.7) or drug-using parents (AOR=1.8;1.5-2.2), girls (AOR=1.6;1.3-1.9), Jewish youth (AOR=1.5;1.2-1.9) and victims of terrorist attacks (AOR=1.4;1.1-1.8). The mean age of first inhalant use was 12.3 (SD=2.8) for boys and girls, which is younger than for all drugs. Students in 7th-8th grades were nearly 4-times more likely than 11th-12th graders to have used inhalants before the age of 12 (AOR=3.8;2.5-5.8). Past-month illicit drug use was more common among past-month inhalant users. This association was particularly strong in Arab boys (OR=5.9;3.4-10.1), but was also significant in Jewish boys (OR=2.9;2.0-4.3), Arab girls (OR=2.8;2.8-6.0) and Jewish girls (OR=2.0;1.5-2.9) (Breslow-Day test of odds ratio heterogeneity across the four groups=0.012).

**Conclusions:** Inhalant use has increased dramatically over the past decade among Israeli youth, and serves as a gateway to illicit drug use. In Israel, where illegal drug use is relatively uncommon, the finding that nearly 15% of school-youth used inhalants in the past year is alarming. Given the lack of awareness of their potential deleterious effects, further research and prevention efforts are warranted, including enhancing the knowledge and awareness of youth, parents, teachers and health care providers.

**Support:** The survey was carried out by the Anti-Drug Authority of Israel

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**DELIVERING PREVENTION FOR ALCOHOL AND CANNABIS OVER THE INTERNET.**

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**Aims:** To establish the efficacy and feasibility of the Climate Schools: Alcohol and Cannabis course, an internet based prevention program for alcohol and cannabis use in adolescents.

**Methods:** Design: A cluster randomised control trial. Intervention and control groups were assessed at baseline, immediately post and at six months follow-up. Participants: 764 13-year olds from ten secondary schools in Sydney, Australia. Half the schools were randomly allocated to the computerised prevention program (n=397 students), and half to their usual health classes (n=367 students). Intervention: Computerised, evidence based, curriculum consistent lessons were developed to reduce alcohol and cannabis use. The 6 lessons on alcohol were given at the beginning of the year and the 6 lessons on alcohol and cannabis use were given 6 months later.

Measures: Alcohol and cannabis knowledge, expectancies and attitudes, alcohol consumption (frequency, quantity and bingeing), frequency of cannabis use, and harms associated with one's use of alcohol and cannabis were assessed at baseline, the end of the course and six month follow-up.

**Results:** There were significant improvements in knowledge regarding alcohol and cannabis use at end of course and at the 6 month follow-up. Frequency of drinking to excess was reduced immediately after the intervention, and average weekly alcohol consumption and frequency of cannabis use was reduced at the 6 month follow-up.

No differences between groups were found on alcohol expectancies, cannabis attitudes, or harms related to alcohol and cannabis use.

**Conclusions:** The Climate Schools: Alcohol and Cannabis course is acceptable and scalable, and fidelity is ensured. It increased knowledge regarding alcohol and cannabis, and decreased use of these drugs.

**Support:** The development of the Climate Schools: Alcohol and Cannabis course was funded by the Australian Government Department of Health and Ageing, and the Alcohol Education and Rehabilitation Foundation.

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**EFFECTS OF CHRONIC MODAFINIL ON COCAINE AND FOOD SELF-ADMINISTRATION 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 pharmacotherapy for cocaine treatment. Modafinil, a mild CNS stimulant currently marketed for the treatment of sleep disorders, shares discriminative stimulus effects with cocaine in rhesus monkeys. Some clinical studies have identified modafinil as a potential medication for treating stimulant abuse disorders. The current study was conducted to examine the effects of chronically administered modafinil on cocaine and food self-administration in adult rhesus monkeys.

**Methods:** Monkeys were trained to self-administer cocaine and food during alternating periods under a second-order schedule of reinforcement seven days per week. Modafinil was administered once every 20 minutes for 23 hours each day into one lumen of a double-lumen intravenous catheter. Self-administration of several doses of cocaine was evaluated during chronic treatment with modafinil. Each cocaine dose was available for at least seven days of self-administration.

**Results:** Thus far, modafinil appears to reduce self-administration of moderate and higher doses of cocaine without affecting food-maintained responding. These preliminary results in rhesus monkeys indicate that modafinil may be effective for reducing cocaine self-administration without altering food self-administration.

**Conclusions:** The findings of this study suggest that modafinil may serve as an agonist-type therapy for treating cocaine dependence disorders.

**Support:** This research was supported by R01-DA002519 (NKM) and K05-DA00101 (NKM) from the National Institute on Drug Abuse, NIH.

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**COPING STYLES OF SUBSTANCE ABUSERS SEEKING ORGAN TRANSPLANTATION.**

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**Aims:** Substance abusers must achieve 6 months of abstinence prior to organ transplantation. Thus, it is essential to identify factors impacting abstinence. Negative coping has been shown to increase the likelihood of relapse, with drug users displaying poorer coping and worse outcomes than alcohol (only) users. With this in mind, the current study sought to characterize coping for patients who were denied transplant due to substance abuse, while comparing coping for those with alcohol (only) problems vs. those with drug problems.

**Methods:** At baseline, 41 patients who were denied liver/renal transplant due to substance abuse completed the Millon Behavioral Medicine Diagnostic. The MBMD measures coping styles including: Introversive, Inhibited, Dejected, Cooperative, Sociable, Confident, Nonconforming, Forceful, Respectful, Oppositional and Denigrated. Scores  $\geq 75$  are considered problematic. Participants were grouped by past year substance use as "Alcohol only" (N=13), or "Drug use" with/without alcohol use (N=28), based on self-report on the Health and Behavioral Issues Test (HABIT) and toxicology screening.

**Results:** Most patients were middle-aged (M=48/10), disabled (66%), males (83%) seeking liver transplant (71%). Thirty-six percent had an Introversive coping style and 32% a Respectful coping style; 21% each had a Dejected, Cooperative, and Denigrated coping styles. No significant differences in coping were found for patients with alcohol (only) vs. drug problems.

**Conclusions:** Some participants demonstrated problematic coping, although no differences were seen in coping for alcohol vs. drug users. This may be due to sample homogeneity, as participants had similar medical and demographic backgrounds. Further examinations of coping behavior and substance use in medically ill populations are warranted.

**Support:** Supported by NIDA/NIH DA015772

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### D-CYCLOSERINE DELAYS REACQUISITION OF COCAINE SELF-ADMINISTRATION BY AUGMENTING CONSOLIDATION OF EXTINCTION LEARNING.

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**Aims:** Acute injection of D-cycloserine (DCS) given pre-extinction training facilitates cocaine cue extinction learning and delays reacquisition of cocaine self-administration by up to 8 sessions in rats. The present study investigated if the observed benefit of DCS on reacquisition was related to extinction consolidation and whether or not extinction training was required to observe a delay in reacquisition.

**Methods:** Rats were trained to self-administer cocaine (0.3 mg/kg) paired with a discrete stimulus light. Vehicle or DCS (30 mg/kg) was injected: 1) following an extinction training session (no cocaine, but cues and levers present); or 2) prior to a no-extinction training session (cocaine, cues and levers not present). To examine the impact of arousal on post-extinction training effects of DCS, rats were either handled for 3 min or immediately returned to their homecages. Reacquisition of cocaine self-administration began 5 days later under conditions identical to self-administration training.

**Results:** DCS injected post-extinction training in combination with brief handling resulted in delayed ( $p < 0.05$ ) reacquisition of cocaine self-administration by up to 2 sessions. However, when injected post-extinction training without handling, DCS failed to delay reacquisition. Rats receiving DCS or vehicle without extinction training also showed an immediate reacquisition of cocaine self-administration.

**Conclusions:** DCS may facilitate encoding and consolidation of cocaine cue extinction learning. Consistent with the view that consolidation requires emotional arousal, it is noteworthy that the benefit of DCS was most pronounced when injected under conditions of high emotional arousal (DCS + extinction responding), less pronounced under conditions of moderate emotional arousal (extinction responding + DCS + handling), and absent under conditions of minimal emotional arousal (extinction responding + DCS + no additional handling) or when extinction training was not provided (DCS + no-extinction training).

**Support:** Supported by DA024315

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### UP-REGULATION OF BRAIN-DERIVED NEUROTROPHIC FACTOR IN THE VENTRAL TEGMENTAL AREA INDUCES FOSB/ΔFOSB IMMUNOREACTIVITY IN MESOLIMBIC PROJECTIONS AND FACILITATES SENSITIZATION AFTER SOCIAL STRESS.

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**Aims:** Brain-derived neurotrophic factor (BDNF) contributes to neuroadaptation induced by psychostimulant administration and is co-localized in dopamine neurons in the ventral tegmental area (VTA). Repeated administration of psychostimulants produces also induction of the transcription factor ΔFosB in the mesolimbic system. We recently showed that repeated social stress exposure produces prolonged increases of VTA BDNF and FosB/ΔFosB expression in mesocorticolimbic regions. These neurochemical alterations were accompanied by long-term cross-sensitization to amphetamine. However, whether mesolimbic BDNF is involved in enhanced drug vulnerability after social stress is unknown.

**Methods:** We used an adeno-associated viral (AAV) vector to overexpress VTA BDNF, which induced BDNF expression for weeks in male Sprague-Dawley rats. Two weeks after AAV-BDNF or control vector infusions, rats were exposed to a single episode of social defeat stress, consisting of an encounter with an aggressive Long-Evans rat.

**Results:** Normally, a single social defeat produces short-term cross-sensitization to amphetamine (about 5 days), whereas repeated social stress induces persistent sensitization. In our experiment, rats were challenged with amphetamine (1.0 mg/kg) 2 weeks and 5 weeks after stress. The combination of stress and enhanced VTA BDNF increased locomotor activity in response to amphetamine 5 weeks after stress, indicating facilitated sensitization. Immunohistochemical labeling revealed that rats with VTA AAV-BDNF exhibited increased FosB/ΔFosB immunoreactivity in the n. accumbens and amygdala, with a tendency towards further augmentation of FosB/ΔFosB labeling in the n. accumbens shell of stressed rats.

**Conclusions:** This suggests that enhanced VTA BDNF expression and social stress may interact to produce long-lasting molecular events consistent with increased vulnerability to psychostimulants.

**Support:** Support: USPHS awards DA24817, DA022830, MH073930.

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### ETHNIC DIVERSITY OF OPRM1 GENE PROMOTER DNA METHYLATION AND ITS ASSOCIATION WITH SUBJECTS IN METHADONE TREATMENT.

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**Aims:** We hypothesize that methylation of specific CpG dinucleotides in the μ-opioid receptor gene (*OPRM1*) promoter region between former severe heroin addicts stabilized in methadone maintenance treatment and control subjects will depend upon ethnicity.

**Methods:** DNA methylation analysis of the μ-opioid receptor gene (*OPRM1*) promoter region was performed by direct sequencing of bisulfite-treated DNA. DNA was obtained from lymphocytes of African Americans (103 cases, 73 controls) and Hispanics (120 cases, 58 controls) and these results were compared to a similar Caucasian cohort in an earlier study.

**Results:** In African Americans, the degree of methylation was decreased significantly experiment-wise in the former heroin addicts at the +12 CpG site ( $p=0.0032$ , Bonferroni corrected general estimating equations). In Hispanics, hypermethylation was found in the former heroin addicts at the -25 ( $p<0.001$ , corrected), -14 ( $p=0.001$ , corrected), and +27 ( $p<0.001$ , corrected) CpG sites. As reported earlier, the -18 site was increased significantly in Caucasian former heroin addicts ( $p=0.048$ , corrected). When the level of methylation in each ethnicity between males and females was compared, no experiment-wise significant difference was found.

**Conclusions:** Altered methylation of the *OPRM1* promoter region in the lymphocytes of former heroin addicts who are stabilized in methadone maintenance could lead to changes in expression. This study may reveal additional mechanisms involved in the causes or the effects of opiate addiction, or its effective treatment.

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### AN IN VITRO PHARMACOLOGICAL MODEL OF MAINTAINED AGONIST SELF-ADMINISTRATION.

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**Aims:** A simple theoretical in vitro model of the PK/PD principles regulating drug self-administration behavior in animals is presented. A model of maintained self-administration of cocaine in rats, the core being the equation  $T = \ln(1+Du/Dst)/k$ , relates the time between injections (T) to the drug unit dose (Du), the minimum maintained drug concentration (Cmin, termed the satiety threshold (Dst) in animals) and the drug first-order elimination rate constant (k). The mechanistic implications of this model are not widely appreciated.

**Methods:** The set up of the proposed "thought experiment" consists of three main parts: 1) an isolated smooth muscle preparation that contracts in response to an agonist. The tissue is maintained in an organ bath in Krebs solution and is attached to a lever that indicates the magnitude of its contraction/relaxation. 2) An actuator, upon contact by the lever, activates a syringe pump that delivers a unit dose of agonist. 3) The agonist is continuously washed out of the organ bath by a constant perfusion with Krebs solution, which mimics first-order elimination kinetics. When the muscle relaxes to a specified length the lever contacts the actuator, which results in the injection of a dose of agonist into the organ bath. The muscle contracts, raising the lever and disconnecting the actuator. As the agonist concentration declines by washout, the tissue relaxes until the lever again contacts the actuator, a dose of agonist is injected and the muscle contracts again. The regular cycle of agonist injections repeats indefinitely.

**Results:** The output of this system is similar to the maintained self-administration of cocaine by rats under an FR-1 schedule.

**Conclusions:** T increases as a function of Du because of the longer time for higher agonist levels to fall to Cmin. The non-linearity of the function is caused by the more rapid decline in the concentration of agonist at the higher concentrations as dictated by first order elimination kinetics. This simple model illustrates that an apparently complex animal behavior can be explained in terms of basic pharmacological principles.

**Support:** NIDA grants DA14189 and DA018538

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# ALCOHOL, PRESS AND PUBLIC POLICIES IN BRAZIL: CONTENT ANALYSIS OF NEWSPAPER AND MAGAZINE STORIES IN 2006 COMPARED TO 2003 AND 2000.

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**Aims:** Aiming at studying the relation between health, press and public policies on Alcohol in Brazil, this research analyses the journalistic texts about alcoholic beverages published in the Brazilian press in 2006, compared to 2003 and 2000.

**Methods:** In the clipping process of eight newspapers and magazines, we selected texts about alcohol. They were submitted to content analysis with a focus on headlines, journalistic classification, sources of information, negative consequences and public policies. The frequency of the texts in 2006 was compared to that of 2000 and 2003 by chi-square test for trends.

**Results:** The frequency of the texts in 2006 (N=139) was higher than that in 2003 (N=86) and 2000 (N=43). In 2006, most of the texts (61%) were "long texts" as opposed to the "short texts" that were more frequent in the previous years. The frequency of texts on accidents increased from 2000 (n=7) to 2003 (N=26) and 2006 (N=55). In 2006, out of the 73 texts that discussed solutions to the issue, 36 focused on public policies, 24 on prevention and 11 on treatment. The most frequent headlines in 2006 were about drinking and driving.

**Conclusions:** The results point to a growing discussion on alcohol public policies, especially regarding traffic accidents. In addition, in 2007, the first National Alcohol Public Policy was approved and, in 2008, a stricter law about drinking and driving was enforced. According to the agenda-setting theory, it is possible to assume that the changes in the approach of the Brazilian media might have boosted alcohol control/prevention policies in Brazil.

**Support:** FAPESP (Fundação de Amparo a Pesquisa do Estado de São Paulo)

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# INITIATING AND MAINTAINING SMOKING ABSTINENCE VIA THE INTERNET.

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**Aims:** Traditional smoking contingency management (CM) interventions are modestly effective in urban populations; however, daily monitoring and reinforcement for continuous smoking abstinence may be impracticable in rural populations. A CM intervention was developed wherein remote real-time videos of smokers providing CO samples were collected via the Internet. The purpose of the present study was to examine the efficacy of this remote smoking CM intervention to initiate and promote smoking abstinence in rural smokers.

**Methods:** The study employed a 6-week, randomized, yoked control design. Subjects were randomly assigned to one of two parallel groups, Abstinence-contingent Group (AC, n=32) or Yoked Non-contingent Group (NC, n=29). Subjects were required to provide CO samples twice daily via video monitoring over the Internet for a 6-wk period. AC group received monetary vouchers for providing CO samples showing recent abstinence (<5 PPM); NC group received vouchers independent of their smoking status.

**Results:** Twice-daily CO collection rates were comparable between the groups at each intervention week with an overall collection rate of 61% for all subjects. Over the 6-wk intervention, 34% of all breath samples were negative (<5 PPM) for the AC group and 10% were negative for the NC group (p<0.05). Abstinence rates were also significantly different between the groups during the last week of the intervention (AC=31%, NC=12%; p<0.05). In addition, 25% of the AC group achieved at least 2 weeks of continuous abstinence, whereas no subjects in the NC group achieved this level of abstinence (p<0.05).

**Conclusions:** These results demonstrate that remote delivery of CM yields good subject compliance and is feasible and efficacious in rural smokers.

**Support:** NCI R21CA12488 (WWS)

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# THE PREVALENCE AND ONSET OF ALCOHOL USE DISORDERS DURING OLDER ADULTHOOD: FINDINGS FROM A 3-YEAR NATIONAL STUDY IN THE UNITED STATES.

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**Aims:** Using a representative study of the U.S., this project estimates the prevalence of past-year alcohol use disorders (AUDs) during older adulthood (age 55+), their onset over a three-year period, and associations with demographic and psycho-social risk factors.

**Methods:** Analyses are based on the subset of older (age 55+) adults (n=10,409) from Wave 1 (2001-2002) and Wave 2 (2004-2005) of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a representative sample of non-institutionalized U.S. adults. Psychiatric diagnoses aligned with common DSM-IV diagnoses were generated using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-version 4 (AUDADIS-IV).

**Results:** The past-year prevalence of AUDs at Wave 1 was 2.2% (approximately 1.3 million older adults), and about 18% of those past-year AUDs reported an age of onset during older adulthood (55+). Over the 3-year follow-up, 1.8% of those with no W1 AUD had onset by Wave 2. Rates of initiation were significantly highest among males, those who were divorced, had an anxiety disorder, and used illicit drugs at W1. Those with significant physical limitations and had a death of a family/friend also had higher rates of onset by W2 compared to those with no physical limitations and did not report the death of a family friend at W1.

**Conclusions:** Even though many of the proportions of older adult AUD onset and past year occurrence appear relatively small, the sheer magnitude of the older adults reaching older adulthood provide insight into the impending demands on the substance abuse treatment system that is likely to occur as the aging Baby-Boom generation reaches older adulthood.

**Support:** Funding for the analyses and writing of this manuscript was provided by NIMH Grant (MH077241, PI: Scott P. Novak) and NIDA Grant (DA020902 PI: Eric O. Johnson).

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# PREGNANT WOMEN IN METHADONE MAINTENANCE: BARRIERS TO TREATMENT AND TREATMENT ENGAGEMENT.

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**Aims:** Substance abuse treatment for pregnant women is critical for the health of both the woman and fetus, and pregnant women face significant challenges that may reduce their access to and effectiveness of treatment. Little research has addressed differences in presenting characteristics and treatment needs in pregnant and non-pregnant women. This study assessed barriers to treatment for pregnant women in methadone maintenance (MM), as well as differences in demographics, drug use patterns, treatment engagement, and treatment outcome between pregnant women (some of whom receive specialized group therapy for pregnant substance abusers) and non-pregnant women who received treatment as usual.

**Methods:** Data were collected from medical records of women entering a MM program from 12/2006 to 12/2008. Pregnant women (n=55) were compared with non-pregnant women (n=73) on demographics, distance traveled to treatment, drug use at admission, percentage of negative urine drug screens across treatment, and percentage of sessions (individual and group) attended.

**Results:** Results indicated that 47% of pregnant women traveled more than 15 miles to the clinic, compared to 14.6% of matched non-pregnant women. Overall, pregnant women had significantly lower group attendance but this difference did not exist when comparing only those pregnant women who attended specialty programming to non-pregnant women. Pregnant women in MM are considered to have high-risk pregnancy and their weekly prenatal medical appointments often interfered with group attendance. Compared to non-pregnant women, pregnant women in this MM program were younger and more likely to have opiate- and cocaine-negative urine drug screens.

**Conclusions:** These results suggest that pregnant women entering MM may present with different characteristics and needs that must be addressed to provide the most effective treatment. A focus on issues relevant to pregnant substance abusers in combination with the development of a social support network with women experiencing similar challenges may increase treatment engagement, and thus lead to improved retention and long-term outcomes.

**Support:** None.



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# INFLUENCES OF MEDICINES, STRESS EVENTS, AND NARCISSISTIC PERSONALITY ON RELAPSE RISK IN JAPANESE ALCOHOL-DEPENDENT INPATIENTS.

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**Aims:** To examine influences of medicines, stress events, and narcissistic personality on relapse risk in Japanese alcohol-dependent inpatients.

**Methods:** Participants and Procedure: One hundred and twenty-four alcohol-dependent inpatients with informed consent answered a questionnaire two weeks after hospitalization. We removed participants who were treated with antipsychotic drugs or anxiolytics except diazepam, or who did not answer the follow-up questionnaire after one month later from the first rating. Data from remaining 31 participants were analyzed with ANCOVA. Measurement: Medicines were diazepam, antidepressants, hypnotics, and alcohol-abuse deterrents. Relapse risks were measured by Alcohol Relapse Risk Scale (Ogai et al, in press). Stress events were also asked, and narcissistic personality was measured by the Narcissistic Personality Inventory-S (Oshio, 1998).

**Results:** Diazepam treatment was significantly and negatively related with emotionality problem (EP) score. Antidepressant treatment was significantly and negatively correlated with total ARRS score and stimulants-induced vulnerability (SV) score, and increased EP score. Hypnotic treatment was significantly and positively related with SV score, significantly and negatively related with positive expectancy for alcohol (PE) score, and increased lack of negative expectancy for alcohol (NE) score. Alcohol-abuse deterrents treatment was significantly and negatively related with total ARRS, SV, and EP scores, and increased NE score. Moreover, stress events significantly increased most of the relapse risks and patients with narcissistic personality reported significantly low risks.

**Conclusions:** Influences of medicines, stress events, and narcissistic personality on relapse risks were shown by the longitudinal ARRS data.

**Support:** This work was supported by grants from the Ministry of Education, Culture, Sports, Science and Technology of Japan (17025054), the Ministry of Health, Labor and Welfare of Japan (H19-Iyaku-023), and the Japan Society for the Promotion of Science (17730421, 17591238).

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# EFFECTS OF VERAPAMIL AND DILTIAZEM IN METHADONE-MAINTAINED HUMANS UNDER A NALOXONE NOVEL-RESPONSE DISCRIMINATION PROCEDURE.

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**Aims:** Previously, we showed that the dihydropyridine calcium channel blocker isradipine (ISR) blocked in a dose-related manner the discriminative stimulus effects of naloxone (NX) in opioid-maintained humans responding under a NX discrimination procedure, producing less than 20% NX-appropriate responding at 5 and 10 mg. The present study examined the efficacy of two prototypic L-type calcium channel antagonists with two different chemical structures, the phenylalkamine verapamil (VER) and the benzothiazepine diltiazem (DLT), in attenuating the behavioral effects of NX in opioid-dependent humans responding under a NX discrimination procedure.

**Methods:** Methadone-maintained subjects were trained to distinguish between a low dose of NX (0.15 mg/70 kg, i.m.; i.e., Drug A) and placebo (i.e., Drug B) under an instructed novel-response drug discrimination procedure, in which subjects identify the drug condition as "A", "B", or "N" (neither A nor B - 'novel'). Once the discrimination was acquired, doses of VER (0, 30, 60, 120 mg) and DLT (0, 30, 60, 120 mg) each alone and in combination with the training dose of NX were tested.

**Results:** Thus far, 4 participants have completed either the entire study (N=2) or at least one test drug-NX dose sequence. VER alone produced predominantly placebo- and some NX-appropriate responding. When administered with NX, VER produced 75, 50, and 75% NX-appropriate responding, respectively, and 0% novel-appropriate responding (n=4). DLT alone produced predominantly placebo- or novel-appropriate responding. When administered with NX, DLT produced 100, 66.7, 100% NX-appropriate responding with 33.3% novel-appropriate responding at the 60 mg dose (n=3).

**Conclusions:** These preliminary results suggest that calcium channel blockers with different chemical structures can be differentiated in terms of their efficacy to attenuate the discriminative stimulus effects of NX in humans, with the current order of efficacy being ISR>>>VER>DLT.

**Support:** Supported by NIDA grant DA10017.

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# DECONSTRUCTING HIV INTERVENTIONS AMONG FEMALE OFFENDERS.

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**Aims:** Female offenders are an important target for HIV interventions. NIDA recently focused an RFA on the interaction of HIV, drug use and the criminal justice system.

**Methods:** Female offenders who participated in the NIDA-funded Prevention of HIV and STDs study were invited to participate in Deconstructing HIV Interventions for Female Offenders. Of the 501 female substance users who participated in the initial study, 129 were initially eligible for participation in the 1-hour mixed-method re-interview. Of those, 97 completed the re-interview. Four sets of standardized ranked questions on intervention preferences were evaluated among women who perceived no drug related risk (n=59) compared to those who perceived drug related risk (n=38). HIV intervention preferences were similar among both groups.

**Results:** Staying out of jail was the most important reason for participating among almost half the women, regardless of risk perception (risk=50%, no risk=42%), followed by learning something (risk=16%, no risk=20%). "Getting paid" was only ranked by 1 woman as the most important factor for participation. In terms of barriers to participation, women who perceived risk most often ranked being turned into police as the greatest barrier (29%), followed by being scared of HIV testing (22%), while those who perceived no risk most often ranked being scared of testing (32%), and no transportation (20%) as the most significant barriers. Availability of childcare was the least frequently ranked barrier to participation. Women in both groups most frequently indicated that they disliked being scared to get test results (risk=29%, no risk=25%). Despite being afraid of being tested and receiving the results, women in both groups most frequently ranked free testing the most favorable aspect of being in a study (risk=37%, no risk=32%).

**Conclusions:** Female offenders, a vulnerable population for HIV and drug use, have complex perceptions related to HIV interventions. The presentation will further detail these women's perceptions, with in depth quantitative and qualitative data.

**Support:** DA11622; PI: Cottler  
DA19199; PI: Cottler

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# AVAILABILITY AND USE OF CLUB DRUGS IN NEW YORK CITY: A MULTI-LEVEL ANALYSIS.

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**Aims:** Data are sparse on club drug use (CDU) and availability among poor, urban, racially diverse populations. Few studies have examined neighborhood-level determinants.

**Methods:** A community-based sample of non, current and former drug users aged ≥18 years were recruited from target neighborhoods in New York City (NYC). CDU and availability (defined as ecstasy, LSD, PCP, GHB, ketamine and methamphetamine) was assessed through an interviewer-administered questionnaire. Neighborhood-level composition (proportions black, Hispanic, white, <poverty level, and aged ≥25 with HS education and median household income) was derived from the 2000 U.S. Census. Binary GEE regression was used to examine the relation between neighborhood factors and CDU and availability.

**Results:** To date, of 1589 people recruited, 38.0% were Hispanic, 49.6% were black and 12.4% were white/other race. The sample was 66.1% male; median age was 40. In terms of lifetime CDU, PCP was the most frequently reported (38.8%), followed by LSD (32.4%), ecstasy (19.8%), and methamphetamine (7.1%). CDU in the last 6 months was reported by 17.2%, with PCP (5.7%), ecstasy (5.3%), and LSD (2.4%) reported most frequently. Ecstasy was the most frequently reported (24.3%) club drug available in the neighborhood of residence followed by PCP (21.3%), LSD (12.0%), and methamphetamine (9.9%). Neighborhood compositional factors were not significantly associated with either CDU or availability after adjustment for individual-level covariates (i.e., age, race, gender, sexual identity, and education).

**Conclusions:** These data demonstrate that club drugs are available in poor NYC neighborhoods. Neighborhood compositional factors (e.g., who lived in the neighborhood) were not significantly associated with CDU or availability. Additional analysis is underway to examine neighborhood contextual factors (e.g., what happened in the neighborhood).

**Support:** This study was partly funded by grants DA018061, DA017020, and MH068192 from the National Institute on Drug Abuse and the National Institute of Mental Health.

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### DEVELOPMENT OF AN INDIRECT SCREENER FOR PERINATAL DRUG USE (WAYNE INDIRECT DRUG USE SCREENER).

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**Aims:** Under-reporting of drug use is common, particularly in the perinatal period (Ostrea et al., 2001). Indirect approaches to identification, focusing on non-face-valid correlates of the target behavior, have shown utility in other settings. For drug use, however, indirect approaches have not been developed using ideal test construction and validation methods, nor have they focused on the perinatal period. The Wayne Indirect Drug Use Screener (WIDUS) is being developed to meet this need.

**Methods:** A total of 181 low-income, primarily African-American women were recruited during post-partum hospitalization. Each woman anonymously completed an investigational battery with items tapping correlates of illicit drug use (e.g., smoking, depression, trauma). Thereafter, they were asked to provide hair and urine samples for drug assays. The present study tested the WIDUS against drug use in late pregnancy as documented by urine and/or hair analysis.

**Results:** ROC curve analysis for 24 selected WIDUS items yielded an area under the curve of .82. At a cut-score of 5, sensitivity and specificity were .83 and .68; positive predictive value was .44, with a negative predictive value of .93. In contrast, and despite anonymity, direct measures of drug use were less sensitive; more than half of all drug-positive women, despite anonymity, denied any drug use in the 3 months prior to pregnancy.

**Conclusions:** While cross-validation is needed, findings support the draft WIDUS as a perinatal drug use screener. A Phase I clinical trial is currently pairing the WIDUS with a brief, indirect, computer-delivered intervention designed to reduce drug use—without presuming that use is present—by engaging participants in a broad discussion of potential parenting challenges, one of which happens to be drug use. If effective, this strategy could facilitate translation of research in screening and brief intervention to real life practice settings.

**Support:** National Institute on Drug Abuse (DA018975)

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### THE IMPACT OF THE INMATE PRE-RELEASE ASSESSMENT ON RURAL INMATE'S 12-STEP ATTENDANCE AND TREATMENT ENTRY.

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**Aims:** According to the Bureau of Justice Statistics the majority of inmates are alcohol or drug involved, indicating a population with sizeable treatment needs. Some individuals receive treatment while incarcerated; however, it is unknown if these substance users are achieving a continuum of care when re-entering rural communities which have limited treatment services.

**Methods:** This study uses data from CJDATS' Inmate Pre-Release Assessment (IPASS), which takes into account 107 rural inmates' historical drug use and criminal activity as well as their performance during the prison-based treatment program to develop a post-release risk measure (i.e., either needs intensive or non-intensive treatment after release). IPASS will be used to predict 12-step attendance and treatment entry within 6 months of release from prison.

**Results:** Participants were primarily white (87%), male (93%), and the mean age was 35 years. IPASS scores indicated that 52% of rural offenders needed intensive treatment upon community re-entry. In bivariate analyses, rural client's with an intensive aftercare placement recommendation, as compared to those with a non-intensive aftercare placement recommendation, were significantly younger, more likely to have ever injected drugs, and had more extensive incarceration histories. The variables which were significant at the bivariate level were entered into two logistic multivariate models predicting 12-step attendance and treatment entry within 6 months of being released from prison; however, having ever injected drugs was the only significant variable. Specifically, re-entering offenders who had injected drugs were more likely to have attended a 12-step meeting (OR: 3.53, 95% CI: 1.09, 11.44) but less likely to have entered treatment (OR: .40, 95% CI: .13, .96).

**Conclusions:** Findings from this study suggest a limited continuum of care for offenders re-entering rural communities and provide implications for rural substance abuse treatment.

**Support:** This research was supported by the National Institute on Drug Abuse (U01-DA016205; K01-DA021309).

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### RECREATIONAL USE OF BENZYLAMINE: A NATIONAL CROSS SECTIONAL SURVEY AMONG CHILDREN AND YOUTH IN STREET CIRCUMSTANCES IN BRAZIL.

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**Aims:** Benzylamine is an anti-inflammatory medicine largely used in pediatrics. This study aims describe the recreational use of benzylamine among children and adolescents in street circumstances in Brazil, alerting to its potential misuse in this and others contexts.

**Methods:** A national cross sectional survey was carried out in 93 welfare services for street youth in 27 Brazilian states capitals. 10 to 18-years-old youth in street circumstances were interviewed using a WHO questionnaire to non-student youth for substance use.

**Results:** Among 2807 respondents, 78 reported a lifetime recreational benzylamine use, the majority of these (85.9%; N = 67) were specifically identified in three Brazilian capitals located in the Northeast of Brazil, the poorest region of the country. Among the 30 respondents who reported recent use of this drug (in the month preceding the survey) 66.7% (N = 20) took the drug in 4 days or more in the month preceding the survey and 36.7% (N = 11) associated this drug with another substance in an attempt enhance psychotropic effects, mainly alcoholic beverages. The intake in each occasion ranged from 100 to 2000 mg of benzylamine. The most used pharmaceutical form was the oral solution. The most frequent (50%) pleasure effects were hallucination and nonspecific sensory changes like "trips". Unwanted effects were reported by 75% of respondents, mainly nausea and vomiting (21.4%). In the majority of the cases the drug was obtained in drugstores without medical prescription presentation.

**Conclusions:** This study identifies the recreational use of benzylamine among children and adolescents in street circumstances in Brazil. This finding also indicates the need for special controls on the prescription and dispensation of this substance. More studies are needed, preferably using qualitative methods, to allow an in-depth investigation into the nuances of the benzylamine culture.

**Support:** SENAD and AFIP

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### SATISFACTION WITH METHADONE TREATMENT CENTERS OF HEROIN-DEPENDENT PATIENTS WHO SHOW POOR RESPONSE TO THIS TREATMENT.

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**Aims:** The present ongoing study is aimed to compare heroin-dependent patients with poor vs. good response to methadone maintenance treatment (MT) in regard to satisfaction with MT centers.

**Methods:** Poor response to MT was defined as voluntary admission in a close addiction unit due to compulsive use of heroin, cocaine, alcohol, benzodiazepines and/or cannabis. Good response to MT was defined as non-use of heroin and cocaine according to periodical urinalysis and, non-compulsive use of alcohol, benzodiazepines and cannabis according to self-report and clinical follow-up. Patient satisfaction with MT was assessed using the Verona Service Satisfaction Scale for MT (VSSS-MT). Scores of VSSS-MT range from 1 (terrible satisfaction) to 5 (excellent satisfaction). The four subscales of VSSS-MT assess patient satisfaction with basic interventions, specific interventions, social worker skills and psychologist skills.

**Results:** Mean overall satisfaction in poor responders (n = 60) was lower than in good responders (n = 19) to MT ( $3.5 \pm 0.7$  vs.  $4.1 \pm 0.4$ ; U Mann-Whitney = 266.0, P = 0.001). Moreover, poor responders scored lower than good responders on VSSS-MT subscales of basic interventions ( $3.7 \pm 0.8$  vs.  $4.2 \pm 0.5$ ; U Mann-Whitney = 334.5, P = 0.018) and specific interventions ( $3.1 \pm 0.7$  vs.  $3.9 \pm 0.5$ ; U Mann-Whitney = 133.5, P < 0.001).

**Conclusions:** Poor response to MT is associated with low patient satisfaction with MT centers.

**Support:** Supported by FIS grant PI060531

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**AMYGDALA VOLUMES AND CRAVING IN ADOLESCENT MARIJUANA USERS.**

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**Aims:** Amygdala volume abnormalities have been reported in relation to craving in alcohol and cocaine dependent individuals, but it remains unclear if these effects are seen in adolescent marijuana (MJ) users, particularly following abstinence. The aim of this study was to understand the relationship between amygdala volume and craving during one month of monitored abstinence in adolescent MJ users.

**Methods:** MJ-using (n=17) adolescents aged 16 to 19 were recruited from local schools. As part of a larger study on brain function in teen drug users, craving measures were collected twice a week throughout a 28-day abstinence period. High-resolution anatomical MRI data were collected at the end of the 28 days. Left and right amygdalas were traced by hand by three trained research assistants; inter-rater reliability was >.86. Composite scores for craving and withdrawal symptoms throughout the 28-day abstinence period were calculated to provide measures of total craving, mood, sleep, and somatic complaints.

**Results:** After 28 days of abstinence, increased craving was significantly associated with smaller left (t=-3.26, beta=-.71, p<.01), right (t=-2.96, beta=-.66, p<.02), and total (t=-3.38, beta=-.71, p<.008) amygdala volumes, after controlling for years of regular drinking and marijuana use, recent cigarette smoking, gender, family history of substance use disorders, in adolescent MJ users. Other measures of withdrawal (i.e., mood, somatic complaints and sleep problems) were not related to amygdala morphometry.

**Conclusions:** These results are consistent with previous literature of adult alcohol and cocaine dependent individuals, who demonstrated reduced amygdala volumes related to higher reports of craving. Interestingly, these relationships were observed independent of gross amygdala abnormalities in these adolescent MJ users (McQueeny et al., in prep). Future studies will examine amygdala morphometry longitudinally to determine if these brain-behavior relationships predict a more severe course of MJ use disorders in these adolescents.

**Support:** Sponsored by NIDA R01 DA021182(Tapert) & F32 DA020206(Medina)

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**METHAMPHETAMINE USE AND SEXUAL HIV RISK BEHAVIOUR IN CAPE TOWN, SOUTH AFRICA: A REVIEW OF DATA FROM 8 STUDIES (2004-2007).**

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**Aims:** Community studies and studies of admissions to drug treatment centers have shown a dramatic increase in the prevalence of methamphetamine use in Cape Town since 2003. Over time the Western Cape province has also seen a dramatic increase in the prevalence of HIV cases among women attending public antenatal clinics. The purpose of the study was to review research conducted in Cape Town between 2004 and 2007 on the link between methamphetamine use and sexual HIV risk behaviour.

**Methods:** A systematic review of published research conducted in Cape Town between 2004 and 2007 was undertaken using PubMed. The reviewers also included unpublished research undertaken by members of the research team.

**Results:** Eight studies, both quantitative and qualitative, were identified focusing on diverse populations, such as learners in school, out of school youth, adults in the community, men who have sex with men and female street sex workers. Methamphetamine was fairly consistently associated across multiple studies with early vaginal sex (4 studies), using alcohol and other drugs before sex (4), having multiple partners (3), and trading sex for drugs (3). Some racial differences were noted in the direction of the association.

**Conclusions:** The consistency of the findings across studies highlights the increased risk for contracting HIV among methamphetamine users in a part of the world with an already increasing prevalence of HIV, and highlights the urgency of targeted interventions aimed at young people and other sectors of the population. The need for further research (particularly focusing on poly-drug use, causal linkages, quantity of methamphetamine consumed and gender differences) is also considered.

**Support:** European Union, CDC, NIDA

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**CRACK COCAINE USE AMONG MONTREAL STREET YOUTH.**

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**Aims:** In Canada, substance misuse and its negative impact on the health of SY is a serious public health concern. Crack cocaine use is suspected to be increasing in downtown Montreal. This study estimates the prevalence and the incidence rate of crack cocaine use among Montreal SY.

**Methods:** Starting in July 2001, SY aged 14-23 years old were recruited into a prospective cohort study. Semi-annual interviews, conducted until December 2005, included completion of an interviewer-administered questionnaire addressing socio-demographic characteristics as well as sexual and drug use behaviours. Proportions of SY reporting lifetime and recent (last 6 months) crack cocaine use were calculated based on data collected at baseline. Incidence was calculated using person-time methods and was based on data collected during follow-up; 95% confidence intervals (95% CI) were calculated.

**Results:** A total of 858 youth were recruited (69% male, mean age of 20.4 years). Lifetime and recent crack cocaine use were reported respectively by 66.7% (95% CI [63.5-69.9]) and 38.0% (95% CI [34.7-41.3]) of them. At the end of the study, the 241 youth who had never used crack cocaine at baseline and had at least one follow-up questionnaire cumulated 545.2 person-years of at-risk follow-up. Among them, 78 started using crack cocaine during follow-up, for an incidence rate of 143.1/1000 person-years (95% CI [113.5-179.4]).

**Conclusions:** The use of crack cocaine is widespread among Montreal SY, and the number of new users is very high. Given the health risks associated with crack cocaine consumption, future studies should investigate predictors of initiation in order to ultimately identify prevention and intervention leads.

**Support:** The cohort study was funded by Ministère de la santé et des services sociaux du Québec, Health Canada, Direction de santé publique de Montréal and Human Resources Development Canada.

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**GENDER DIFFERENCES IN THE PREVALENCE OF PRESCRIPTION OPIOID USE AMONG INPATIENTS WITH SUBSTANCE USE DISORDERS.**

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**Aims:** High rates of alcohol abuse have been observed in women and men entering treatment for opioid abuse (Cicero et al., 2008). However, little is known about the prevalence of prescription opioid use among treatment-seeking patients with co-occurring substance use disorders.

**Methods:** Rates of prescription opioid use were examined among 103 (58 women, 45 men) inpatients admitted to a short-term substance use detoxification unit. Participants completed a battery of instruments assessing demographic information, prescription opioid misuse, alcohol and other substance use, and Axis I symptomatology.

**Results:** Alcohol and tobacco were the most prevalently used substances. Over one-third (36.1%; 16 men, 19 women) reportedly consumed alcohol daily in the last 30 days. Significantly more men than women (32.9% vs. 21.6%) met criteria for current alcohol abuse (p = .01). Over half (55.7%; 26 men, 28 women) smoked cigarettes daily over the past 30 days.

Overall, 36.7% (43.2% men, 31.5% women) reported currently using prescription opioids and 77.8% (81.8% men, 74.5% women) had used prescription opioids in the past. Men were significantly more likely than women to currently use morphine (p = .000), oxycodone (p = .000), hydrocodone (p = .004), Lortab® (p = .033), and Oxycontin® (p = .001).

**Conclusions:** Significant gender differences in type of prescription opioids and other substance use were revealed. Women were less likely than men to have alcohol abuse or dependence. Although preliminary, the findings help increase understanding of prescription opioid use in patients seeking treatment for other substance use disorders. Clinical implications and suggestions for future research will be discussed.

**Support:** Support: Funding from the NIDA Drug Abuse Research Training (DART) program R25DA020537-02 (PI: Brady, KT).

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### THE RISK AND RESPONSIVITY PRINCIPLES AS MODERATORS OF DRUG ABUSE TREATMENT OUTCOMES: A META-ANALYSIS.

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**Aims:** Evidence-based Principles of Treatment (EPT) is a project using meta-analyses to assess whether NIDA's "Principles of Drug Addiction Treatment" and Andrews and colleagues' "Principles of Effective Correctional Treatment" are supported by treatment outcome studies. We examine two of the Andrews principles. 1) The Risk Principle: intensive treatment should be reserved for clients at high risk of offending. 2) The Responsivity Principle: cognitive-behavioral therapy (CBT) (as opposed to psychodynamic or expressive therapies) are most appropriate to the learning styles of offenders. Programs adhering to these principles are expected to have better outcomes than program that do not. Andrews and colleagues have validated these principles on general offender samples; this analysis sought to determine whether they are supported among primarily drug-abusing clients.

**Methods:** In analyses of subsamples of the EPT database (consisting of over 250 treatment-control comparisons), using meta-analysis techniques, we examined measures of risk and responsivity as moderators of average effect sizes for drug use and crime.

**Results:** For the Risk Principle, high risk for criminal offending was associated with higher effect sizes for drug use and crime outcomes. By contrast, high risk for drug relapse was associated with lower effect sizes for drug use and crime outcomes. For the Responsivity Principle, CBT treatments had higher effect sizes for drug use outcomes than did psychodynamic/expressive treatments. While effect sizes for crime outcomes were higher for CBT treatments than for psychodynamic/expressive treatments, the difference was not significant. Small numbers of studies for some comparisons limited power to detect differences.

**Conclusions:** When applied to studies of drug abuse treatment samples, the Risk and Responsivity Principles do not appear to operate as consistently as with offender treatment samples. Results generally support the use of cognitive-behavioral treatments with substance-abusing clients.

**Support:** NIDA grant R01DA016601

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### EFFECT OF TRAUMATIC EVENT RE-EXPOSURE AND POST TRAUMATIC STRESS DISORDER ON SUBSTANCE USE DISORDER TREATMENT OUTCOMES.

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**Aims:** Very high rates of re-exposure to traumatic events and PTSD are common in SUD patients (Peirce et al. 2008, 2007). In the present study we evaluate the effect of such experiences on treatment outcomes.

**Methods:** We present preliminary results from the first 112 of approximately 300 enrolled participants; the full sample will be presented at the meeting. Participants all received methadone for opioid dependence and enrolled in a parent study that provided access to psychiatric care. Participants were assessed for traumatic event re-exposure every 1 month and PTSD every 4 months. Outcomes included drug urinalysis results and treatment retention.

**Results:** Slightly over half were women (60%; n=67), and the sample was racially diverse (White 54%; Black 32%; other/mixed race 14%). Average age was 40 years (SD=8), and 54% had a high school education. Similar to previous reports, about 20% of the sample reported at least one new traumatic event exposure each month, and 25% of participants met criteria for PTSD at each assessment. Traumatic event re-exposure in one month was not associated with differential rates of drug use in the following month (e.g., Month 1 re-exposed = 49% positive vs. not re-exposed = 41%;  $p > .4$ ). PTSD was not associated with rates of drug use in the following 4 months (e.g., Month 0 PTSD = 50% positive vs. no PTSD = 44%;  $p > .4$ ). With regard to treatment retention, traumatic event re-exposure in any month was not predictive of faster attrition (e.g., Month 1: Beta = -.11;  $p > .2$ ). However, PTSD was associated with attrition. Participants with PTSD at Month 0 left treatment 2 months earlier than participants without PTSD (7.6 months vs. 9.8;  $p < .05$ ). Participants who remained in treatment until Month 4 were similarly at risk for attrition (Month 4 PTSD 10.5 months vs. no PTSD 11.8;  $p < .09$ ).

**Conclusions:** Traumatic event re-exposure, although common, does not necessarily affect patients' response to SUD treatment. PTSD does increase the risk of poor outcomes, primarily by increasing treatment attrition.

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### BRAZILIAN ROADSIDE SURVEY FOR ALCOHOL AND OTHER DRUGS – INTERIM ANALYSIS.

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**Aims:** To estimate the prevalence of alcohol, cocaine, marijuana, benzodiazepines and amphetamines among drivers on federal highways in Brazilian metropolitan state capitals.

**Methods:** Drivers from 27 major metropolitan areas were randomly asked to participate in the study by police officers from 12am to 12pm on Fridays and Saturdays. After consent, trained interviewers collected data including breathalyzer and saliva. We present preliminary data from 1,374 of those who consented, which represents 99% of those asked to participate.

**Results:** The mean age was 36.9±11; 95% were male; 74% had a high school degree; and 52% drove cars, 9% buses, 11% trucks, and 29% motorcycles. 60% drank an average of 7-15 drinks daily; 25% binged at least twice a month; 13% drank on the day of the interview; 24% drove after drinking more than the legal limit in the past year; and 62% had been a passenger with someone who drank. Drivers who drank 7 or more drinks daily were significantly older (mean: 37±11 vs. 35±11); had a higher monthly income and were more likely to have a positive BAC (9% vs. 2%). Drivers who reported drinking above the legal limit were more likely to be single (44% vs. 33%) and less educated. Overall, 6% had a positive BAC. Motorcycle drivers used more cocaine (3%) and marijuana (3%), and truck drivers used more amphetamines (5%).

**Conclusions:** This is the first nationwide study of Brazilian drivers. Although heavy alcohol consumption and DUI were reported, the proportion of positive BACs was lower than expected, possibly due to a zero tolerance law that was recently implemented in Brazil, as well as the time of day when data collection was conducted. Targeted prevention interventions will be discussed including motorcycle and truck drivers.

**Support:** Brazilian Secretariat for Drug and Alcohol Policies

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### OBJECTIVE SLEEP (POLYSOMNOGRAPHY) ON ENTRY TO METHADONE MAINTENANCE TREATMENT AND FOLLOWING 6 MONTHS OF TREATMENT.

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**Aims:** As poor sleep is highly prevalent among MMT patients we evaluated methadone effect on sleep by measuring objective sleep patterns (PSG) of opiate addicts patients on admission to MMT and following 6 months of treatment.

**Methods:** The following measurements were done twice (on entry and following 6 months): Pittsburgh Sleep Quality Index (PSQI) self-report questionnaire, pain self-report questionnaire, routine urine test results for drug abuse (opiates, benzodiazepine, cocaine, cannabis, amphetamines), and one-night PSG recordings.

**Results:** Between November, 2006 and January, 2008, 26 patients did their first PSG and 23 of them repeated PSG 6 month later (the dropouts are one who left treatment, one refused and one in jail). Sleep indices did not change on entry and following 6 months (matched t-test): True sleep time (5.5±1.1hr vs. 5.3±1.7,  $t=0.8$ ,  $p=0.4$ ), sleep efficiency (80.7±10.4 vs. 75.9±19.2  $t=1.2$ ,  $p=0.2$ ), REM % of sleep cycle (14±8.8 vs. 16.6±8.3,  $t=-1.1$ ,  $p=0.3$ ), percentage of stage 3-4 (8.0±9.6 and 11.3±11.9  $t=-1.2$ ,  $p=0.2$ ) and neither in PSQI scores (11.4±4.8 vs. 11.1±5.5  $t=0.3$ ,  $p=0.7$ ). BDZ was abused "always" (month 1 and month 6) among 11(47.8%), once among 10 (43.4%) and, "never" among 2(8.7%) patients. Stage 3-4 was missing at least once among 10(90.9%), 5(50%), and 0(0%) respectively ( $p=0.01$ ). BMI increased significantly (24±4.2 and 25.7±4,  $t=-4$ ,  $p=0.001$ ). Mean methadone dose at 6 month was 133.5±31.1 mg/d and its serum level 437.7±170.3ng/ml, which both correlated (Pearson  $R=0.5$ ,  $p=0.05$ ).

**Conclusions:** Opiate addicts suffer from poor objective and perceived sleep on entry to MMT, and methadone doesn't affect patients' sleep following 6 month of treatment. The highly prevalent BDZ, strongly associated with poor sleep. Immediate intervention to help patients cope with their sleep problem is recommended. Bigger sample size and longer follow up is needed.

**Support:** The study was supported by the Israel National Anti-Drug Authority and The Adelson Family Foundation

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# PHARMACOKINETIC PROFILE OF LISDEXAMFETAMINE DIMESYLATE AFTER 14-DAY INTRANASAL ADMINISTRATION IN DOGS.

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**Aims:** To compare the pharmacokinetic (PK) profiles of lisdexamfetamine dimesylate (LDX, Vyvanse®, Shire US Inc) and immediate-release d-amphetamine sulfate (d-AS), after 14-day intranasal (IN) administration in dogs. We hypothesized that systemic exposure to d-amphetamine would be lower after IN LDX than IN d-AS.

**Methods:** Male and female beagles (n=24; 3/sex/group) received IN LDX 7 mg/d (equivalent amphetamine content to 3 mg/d d-AS), LDX 25 mg/d, d-AS 3 mg/d, or vehicle (0.9% saline) for 14 days. Blood for PK analysis was collected between 5 minutes and 24 hours postdose on days 1 and 14. LDX and amphetamine were quantified by a validated LC/MS/MS method. Descriptive statistics but no formal statistical comparisons were performed. Other assessments included clinical observation, body weights, blood and urine analysis, and pathological evaluations.

**Results:** Systemic exposure to amphetamine after IN LDX (7 mg/d) was lower than after IN d-AS (3 mg/d) for both sexes on days 1 and 14. Mean (SD) C<sub>max</sub> values on day 1 were 29.7 (8.3) and 12.9 (0.7) ng/mL for LDX vs 87.0 (40.6) and 76.8 (39.1) ng/mL for d-AS in females and males, respectively, while AUC<sub>0-24h</sub> values were 180 (43.3) and 132 (20.4) ng•h/mL for LDX vs 218 (67.2) and 198 (7.5) ng•h/mL for d-AS in females and males, respectively. Similar data were obtained on day 14, suggesting a lack of accumulation on repeated dosing. Systemic exposure to LDX and amphetamine increased with increasing IN LDX dose (7 to 25 mg/d), although dose-proportionality could not be assessed. No local or systemic side effects were noted with 7 mg/d LDX or 3 mg/d d-AS. Some transient and/or partially reversible pharmacologic, clinical, or histopathologic effects were noted with LDX 25 mg/d.

**Conclusions:** Systemic exposure to amphetamine was markedly lower after IN LDX vs d-AS given in equivalent doses to dogs in this study. If replicated in humans, these findings may suggest reduced abuse liability of this stimulant pro-drug relative to equivalent d-AS doses, given that elevated d-amphetamine concentrations did not follow IN administration of LDX.

**Support:** Supported by funding from Shire Development Inc.

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# STIMULATION OF MEDIAL PREFRONTAL CORTEX 5-HT2C RECEPTORS ATTENUATES COCAINE SEEKING, BUT NOT COCAINE SELF-ADMINISTRATION.

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**Aims:** 5-HT2C receptor agonists attenuate reinstatement of extinguished cocaine-seeking behavior produced either by cocaine priming or presentation of cocaine-associated cues. The medial prefrontal cortex (mPFC) is densely populated with 5-HT2C receptors, which have been shown to modulate hyperlocomotive and discriminative stimulus effects of cocaine. To further elucidate the role of these receptors in addiction-like processes, this study examined the effects of intra-mPFC microinfusions of the 5-HT2C/2B agonist, MK 212 (0, 0.01, 0.03, 0.1 µg/side), on cocaine self-administration and reinstatement of extinguished cocaine-seeking behavior.

**Methods:** Male Sprague-Dawley rats were trained to self-administer cocaine (0.75 mg/kg, IV) that was paired with light and tone cues. Once stable responding was achieved, we investigated the effects of MK 212 microinfused into the mPFC on maintenance of cocaine self-administration. Subjects then underwent daily extinction training to reduce cocaine-seeking behavior (operant responses without cocaine reinforcement). Once low extinction baselines were achieved, rats were tested for reinstatement of extinguished cocaine-seeking behavior either by cocaine-priming injections (10 mg/kg, IP) or response-contingent presentations of the cocaine-associated cues; operant responses during cocaine-primed reinstatement tests produced no consequences.

**Results:** Intra-mPFC MK 212 microinfusions dose-dependently attenuated both cocaine-primed and cue-elicited reinstatement of extinguished cocaine-seeking behavior without reliably affecting the number of self-administered cocaine infusions. MK 212 administered without either cocaine-priming injections or the presentation of cocaine-associated cues produced no discernable reinstatement.

**Conclusions:** These results are consistent with previous research, and suggest that stimulation of mPFC 5-HT2C receptors attenuates the incentive motivational effects produced either by exposure to drug-paired cues or by sampling cocaine.

**Support:** DA11064

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# ACUTE NEGATIVE AFFECT RELIEF FROM SMOKING MAY BE RELATED TO THE SITUATION AND UNRELATED TO NICOTINE INTAKE.

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**Aims:** Smoking clearly relieves negative affect (NA) caused by smoking abstinence (i.e. withdrawal), and NA after quitting smoking increases risk of relapse. However, it is not clear that smoking acutely relieves NA from sources other than abstinence, such as situational challenges.

**Methods:** This study examined NA relief due to smoking as a function of four validated negative mood induction procedures, one per session: 1) withdrawal (overnight abstinence), 2) challenging computer task, 3) preparation of public speech, and 4) negative mood slides. A fifth session involved a neutral mood control. Nicotine dependent smokers (N=77 to date) were randomly assigned to one of three groups varying in the smoking condition they were exposed to in all 5 sessions: nicotine cigarettes, denic cigarettes, or no smoking. All subjects engaged in the mood induction procedure assigned for that session following baseline rest. The two smoking groups took 4 puffs on the designated cigarette, and then smoked more of those cigarettes ad lib during continued mood induction. All subjects intermittently rated their level of NA on four measures (Mood form, PANAS, Stress-Arousal Checklist, and STAI-state).

**Results:** Smoking very significantly relieved NA due to smoking during withdrawal, but there was little or no NA relief due to smoking during the other three mood induction procedures or neutral mood. NA did not differ between the nicotine and denic smoking groups. By contrast, ad lib smoking in the two smoking groups was greater during withdrawal and speech preparation compared to the other conditions, but the nicotine content of cigarettes made no difference.

**Conclusions:** These findings indicate that smoking acutely relieves NA in only limited situations and may do so regardless of nicotine intake, challenging the common assumption that smoking, and nicotine in particular, broadly alleviates NA.

**Support:** Supported by NIH Grant DA19478.

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# PREVALENCE OF SEVERE PAIN AMONG METHADONE MAINTENANCE PATIENTS.

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**Aims:** The aim of this study was to assess the prevalence of severe pain among methadone maintenance patients and to explore differences between HCV positive patients with and without severe pain in this treatment setting.

**Methods:** Data were collected as part of an ongoing study examining the effectiveness of a hepatitis care coordination model. Participants (n = 138) completed the Brief Pain Inventory (BPI) at two methadone clinics during a baseline assessment. Severe pain was defined as a score of 5 or higher on the item "worst pain in the past week". Pain-related disability was assessed as the average of the 7-items on the BPI pain interference scale.

**Results:** Participants were Caucasian (31%), African-American (29%), Latino (28%), and other (12%). The majority were male (64%), and the mean age was 47 (SD = 9.42). Of 138 participants, 54% had severe pain, and 44% were prescribed an analgesic. Among those with any pain, high levels of pain-related disability (mean score of 5 or higher) was reported by 46%. There was a trend in favor of a higher prevalence of severe pain among HCV positive patients (37% vs. 17%; p = 0.08). Among those reporting any pain in the past week, a greater proportion of HCV positive patients had high levels of pain disability (30% vs. 16%, p < .05).

**Conclusions:** These data indicate that severe pain is prevalent among methadone maintenance patients, and that pain commonly interferes with functioning and quality of life. HCV status is associated with pain prevalence and disability. Methadone maintenance patients, and particularly those who are HCV positive, may have unmet needs for pain management. Further investigations are needed to define these needs and an optimal strategy for pain management in this population.

**Support:** Supported by NIDA R01DA20781, R01DA020841, P30DA011041, and U10DA15815.

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# CHRONIC TOLUENE EXPOSURE DIFFERENTIALLY REGULATES AMINO ACID NEUROTRANSMITTERS IN THE ADOLESCENT RAT BRAIN FOLLOWING ACUTE OR PROLONGED DRUG ABSTINENCE.

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**Aims:** Toluene is an abused inhalant with an exceptionally high incidence of abuse by adolescents. We reported previously that acute toluene exposure decreases glutamate (GLU) and gamma-aminobutyric acid (GABA) in hippocampus, decreases GABA in anterior striatum, and has little effect on amino acid neurotransmitter levels in prefrontal cortex of juvenile rats (postnatal day 21; P21). In this study, the effects of chronic toluene exposure during adolescence on amino acid neurotransmitter levels were determined using proton magnetic resonance spectroscopy *ex vivo* (at 11.7 T).

**Methods:** Male Sprague-Dawley rats exposed to toluene (0, 8000, or 12,000 ppm) for 15 min daily from P28-P34 were euthanized 1 day (P35; acute) or 1 week (P42; prolonged) later to assess whole tissue GLU and GABA levels in prefrontal cortex, anterior striatum and hippocampus.

**Results:** Chronic toluene exposure did not affect striatal GLU or GABA levels after either acute or prolonged drug-abstinence. In cortex, 1 day after chronic toluene, GLU was significantly reduced with no effect on GABA; after 1 week, GLU was unaffected but GABA was significantly increased. In hippocampus, 1 day after chronic toluene GABA and GLU were unchanged but a general decrease was seen in other MR-visible neurochemicals (e.g., glutamine, myo-inositol, N-acetylaspartate); after 1 week a general increase in GABA, GLU, and other MR-visible neurochemicals was observed.

**Conclusions:** These data suggest that chronic toluene differentially regulates amino acid neurotransmitters in the cortex after acute and prolonged abstinence with GLU being affected after 1 day and GABA being affected after 1 week. The effects of chronic toluene in the hippocampus may reflect a general hypo-activity after acute abstinence and a general hyperactivity after prolonged abstinence.

**Support:** NIH/NIDA R21-DA019151 to SEB, R01-DA016736 to MPG, and K01-DA024760 to SAP.

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# STOPPING MARIJUANA INCREASES ALCOHOL USE: AN EXPERIMENTAL VERIFICATION OF DRUG SUBSTITUTION.

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**Aims:** Many drug abuse treatment programs recommend abstinence from all psychoactive substances because clients who stop their use of one drug may substitute another. Research to confirm this notion of substitution is limited. Clinical trial data suggest abstinence from one drug does not increase use of another, but some smokers with a past history of alcoholism relapse to alcohol use during tobacco abstinence. We conducted a within-subjects study to examine whether marijuana users increase alcohol use when they abstain from marijuana.

**Methods:** We recruited 28 marijuana users who met DSM-IV criteria for current cannabis dependence or abuse and were moderate alcohol drinkers. Participants completed a 1-week baseline period in which they used marijuana as usual, a 2-week period in which they abstained from marijuana, and a 1-week return-to-use period. To induce abstinence, participants received vouchers contingent upon urinalysis verification of abstinence.

**Results:** Marijuana abstinence significantly increased alcohol use by 14% (2.6 vs. 2.9 drinks/day,  $p < 0.05$ ). This increase was mostly due to those with a past history of alcohol abuse or dependence; they increased their alcohol use to a much greater degree (2.5 vs. 3.7 drinks/day, a 51% increase) than did those without this history (2.6 vs. 2.7 drinks/day, a 3% increase). Increased alcohol use did not result in a clinically-significant increase in alcohol problems but did increase craving for alcohol. Marijuana abstinence did not increase use of caffeine, cigarettes or illicit drugs.

**Conclusions:** The drug substitution effect appeared to be restricted to alcohol and among those with a past history of alcohol problems. Our results suggest clinicians should closely monitor alcohol use among marijuana users trying to quit, especially those with a past history of alcohol problems. Future research needs to replicate these findings with a sample representative of treatment-seekers for marijuana problems.

**Support:** Research funds from the Department of Psychiatry, UVM; NIDA Training Grant DA-07242(ENP); and NIDA Senior Scientist Award DA-000490(JRH).

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# EFFECTS OF ACUTE NICOTINE ON DELAY DISCOUNTING IN RATS.

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**Aims:** Impulsive choice, defined as preference for a smaller-sooner reinforcer over a larger-delayed reinforcer has been associated with cigarette smoking in humans. In rodents, acute administration of nicotine increased impulsive choice when the delay to the large reinforcer was signaled. Other research has shown that the effects of stimulants on delay discounting vary depending on the presence of a cue during the delay to the large reinforcer. The goals of the present study were to examine the effects of nicotine on impulsive choice using a delay discounting task, and to determine whether signaling the delay to the larger reinforcer altered nicotine's effects.

**Methods:** Adult male Sprague-Dawley rats were trained that a response on one lever yielded 1 food pellet delivered after 1 s, while a response on a second lever yielded 3 food pellets after a variable delay. The delay was initially set to 10 s and was adjusted until the pattern of choices reflected indifference between the two alternatives. In one group, the delay to the larger reinforcer was signaled by a blinking stimulus light, and in a second group, the delay to the larger reinforcer was not signaled. Once choice patterns were stable, nicotine (0, 0.03, 0.1, 0.3, 0.56 and 1.0 mg/kg) was administered 10 min prior to delay discounting sessions.

**Results:** Regardless of stimulus condition, nicotine dose-dependently reduced choice of the larger-later reinforcer from approximately 50% to 15%. The latency to the first response was increased after administration of 1.0 mg/kg nicotine; however, latencies to subsequent responses were unaffected.

**Conclusions:** These findings are consistent with prior animal studies on nicotine-induced impulsivity, and suggest that nicotine increases impulsive choice regardless of the stimulus conditions associated the larger reinforcer.

**Support:** Support: Career development award (M.G.L.) and postdoctoral fellowship (J.L.P.) from the Minneapolis Medical Research Foundation.

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# INTERVENING TO ADDRESS DRUG USE AND SEXUAL HIV RISK AMONG FEMALE SEX WORKERS IN DURBAN, SOUTH AFRICA.

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**Aims:** Between 2005 and 2007 formative work was undertaken to inform interventions aimed at addressing drug use and sexual HIV risk among female commercial sex workers (CSW) in Durban, South Africa. Components of the intervention include building referral networks, decreasing stigma among service providers, influencing NGO practices as well as government drug and HIV policies.

**Methods:** In 2007, in collaboration with a local NGO, an initiative was begun to roll out a number of harm reduction strategies for drug using CSW in Durban. The MRC is responsible for the regular monitoring of activities undertaken by the NGO. Activities include outreach; condom distribution and other preventive interventions; provision of VCT; and referrals to drug, HIV and other services.

**Results:** Over the first 8 months 241 drug-using CSW were reached through outreach that promotes HIV/AIDS prevention and addresses drug risk behaviors and 64 received VCT and their results. At baseline, condom use varied, with 4.1% indicating no condom use at all, 68.7% reported poly-drug use and the number of times that CSW used substances when having sex ranged from 0 to 2700 (median = 672) with only 3.3% not using substances when engaging in sex. Outreach workers assisted CSWs in developing risk reduction strategies. On follow-up, only 2% had managed to stop using drugs while 30.2% had sometimes stopped. Relatively high numbers were able to discuss condom use with partners. Most CSW carried condoms every time they planned to have sex, the majority sometimes decreased or eliminated drug use when having sex (77.9%) and 12.8% did so every time.

**Conclusions:** The intervention to date has demonstrated willingness of the NGO to broaden its service delivery activities and uptake of VCT and other services by vulnerable drug using women. Improved integration of drug treatment, HIV intervention and other services has also occurred. Workshops took place late 2008 to review the efficacy of strategies and inform policy makers about harm reduction approaches that need to be rolled out more broadly for this population.

**Support:** CDC, PEPFAR

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**COCAINE AND WELL-BEING: ENTRIES, EXITS.**

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**Aims:** The research of well-being could be considered a general motivation of entry as well as exit from addiction, which encompasses manifold peculiar motives from depression to venture and hedonism. Desinhibition, mind alertness, efficiency, euphoria are strong characteristics of cocaine effects, with short term highs and painful coming down. On the other hand, anhedony, anxious states, aggressiveness, gloom... are usually reported as typical of cocaine craving. Attempts of interruption are often motivated by serious bodily and social problems threatening the pursuit of a good life.

Our study aims at comparing motivation for the well-being, the structures of the choice and the types and the rhythms of rewards before and after interruption, in order to point out homologies, analogies and differences between the "highs" or the "good times" in both periods.

**Methods:** Work in progress with theoretical considerations from an ongoing study about the motives of recovery and the substitutes of cocaine, with 21 clinical cases analyzed from various disciplinary perspectives (philosophy, psychiatry, hepatology).

**Results:** After interruption, clinical and phenomenological observations show a frequent research of substitutes such as social success, numerous sexual intercourse, overeating, intensive sports, adventurous travels... Some subjects also report new modes of connection with others, more friendly, brotherly and authentic, as well as new political and spiritual commitments. Typically, the temporary self-confidence of consumption can be replaced by feelings of self-esteem, when affective and social links are restored.

**Conclusions:** These observations invite to pay more attention to the ordinary highs of everyday life in their cultural contexts, as possible specific alternatives to intensive and extreme highs of cocaine. Substances users share ordinary motivation for the well-being, which has to be considered in order to improve the incitements for people intending to stop a severe use of cocaine.

**Support:** The present proposition is issued by an interdisciplinary team of two physicians and one social philosopher.

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**DISTRIBUTION OF CHRONIC VENOUS DISORDERS IN A METHADONE-MAINTENANCE TREATED SAMPLE.**

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**Aims:** Infrequently acknowledged as a drug use complication, chronic venous disease (CVD) is likely underappreciated in terms of its magnitude and impact on injection drug users. This study examined the spectrum and severity of CVD and the impact of years and site of injecting on disease progression.

**Methods:** The study was a cross-sectional, comparative design stratified by age, sex, ethnicity, and 3 types of drug use [non-injection (n=195); arm or upper body injection only (n=178); and legs with or without upper body injection (n=340)]. Participants completed demographic, health, and substances abuse questionnaires; their legs were evaluated for CVD using the clinical component of the Clinical-Etiology-Anatomy-Pathophysiology (CEAP) Classification.

**Results:** Participants (N = 713) were 335 men (46.9%) and 378 women; 61.7% were African American. Their mean±SD age was 46.26±9.06 years. Only 7.7% (n = 55) of the sample did not exhibit clinical CVD changes; 56.8% percent had mild CVD; 18.5% had moderate CVD and 17.8% had severe CVD. Persons who injected in the groin, legs, and feet had significantly worse CVD than those who never injected and those who injected in the arms/upper body. Thirty-nine percent of leg injectors versus 4.2% or non-injectors or arm only injectors had moderate to severe CVD. After controlling for age and co-morbid conditions, persons who injected in the legs were 9.14 times more likely to develop venous ulcers than those that injected in the arms and upper body only and 34.64 times more likely as those who never injected.

**Conclusions:** CVD is associated with injecting in the groin, legs and feet as compared to other sites. Leg assessment is crucial for persons who injected drugs. More research is needed to determine earliest signs of advanced CVD.

**Support:** National Institute of Nursing Research/National Institute of Health (NINR/NIH), R01 NR009264.

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**DOSE PREFERENCE AND DOSE ESCALATION OF COCAINE 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 sessions in rats are carried out with a constant unit dose of cocaine throughout the experiment. Cocaine users will escalate the dose when unlimited amounts of cocaine are available. Our aim here was to design a 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, we also compared two rat strains, Fischer and Lewis, which have a lower and higher sensitivity to the rewarding effects of cocaine, respectively.

**Methods:** We used the Fischer and Lewis rats. Rats were trained to self-administer cocaine (0.5 mg/kg/injection) in two-hour daily sessions. The criteria for the acquisition of self-administration were reached after 12 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 different doses of cocaine. 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 cocaine doses were used ranging between 0.2 to 2.5 mg/kg/infusion.

**Results:** After 14 days of exposure to extended self-administration sessions, Lewis rats showed a clear preference for the higher doses of cocaine available, with most of the individuals escalating to the highest dose (2.5 mg/kg/infusion). Fischer rats, however, preferred the lower doses available and very few rats escalated to the highest dose.

**Conclusions:** Our work shows that when different doses of cocaine are available, Fischer rats prefer lower doses of cocaine, while higher doses may be aversive. On the other hand, Lewis escalated to the highest dose available.

**Support:** This work was supported by grants NIH-NIDA P60-DA05130 and The Arcadia Charitable Trust.

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**GABA-A RECEPTOR SUBTYPE MECHANISMS IN THE DISCRIMINATIVE STIMULUS EFFECTS OF ETHANOL IN MONKEYS.**

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**Aims:** Ethanol's ability to enhance GABA neurotransmission via GABA-A receptors has been implicated as an important mechanism underlying its behavioral effects. GABA-A receptors are pentamers comprised of subunits from at least five different families. GABA-A subunits, including alpha1, alpha4, alpha5, and delta, are associated with the reinforcing effects of ethanol. Reinforcing effects depend, in part, on the ability of the drug to engender characteristic subjective effects. In the laboratory, a drug's subjective effects are studied using drug discrimination methods. This study evaluated the role of GABA-A receptor mechanisms in the discriminative stimulus (DS) effects of ethanol using ligands selective for alpha1, alpha4, alpha5, and delta subunit-containing GABA-A receptors.

**Methods:** Monkeys were trained to discriminate ethanol from saline under a fixed-ratio schedule.

**Results:** In substitution studies, the DS effects of ethanol were mimicked at least partially by the alpha1/GABA-A agonists zolpidem, zaleplon and CL218,872 and the alpha5/GABA-A agonists QH-ii-066 and panadiplon. In contrast, gaboxadol, an agonist selective for alpha4/delta-containing GABA-A receptors, engendered saline lever responding up to doses that produced untoward side effects. In antagonism studies, the DS effects of ethanol were attenuated in a dose-dependent manner by Ro15-4513, RY-23 and L-655,708 – inverse agonists exhibiting selectivity for alpha5/GABA-A receptors. Antagonism occurred at doses of the inverse agonists that did not alter response rate, suggesting that the blockade was not the result of nonspecific disruptions of behavior. On the other hand, the DS effects of ethanol were not altered by the alpha1/GABA-A antagonists BCCT and 3-PBC.

**Conclusions:** These results provide support for a key role of alpha5/GABA-A receptor subunits in the DS of ethanol. However, in contrast to their role in ethanol's reinforcing effects, the alpha1, alpha4 and delta receptor subunits appear to not play a central role in ethanol's subjective effects.

**Support:** AA16179, MH46851, RR00168

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**DISASTER PREPAREDNESS FOR DISRUPTIONS IN METHADONE TREATMENT.**Deborah Podus<sup>1</sup>, J C Maxwell<sup>2</sup>; <sup>1</sup>UCLA-ISAP, Los Angeles, CA, <sup>2</sup>University of Texas, Austin, TX

**Aims:** Disaster planning is important for all drug abuse treatment modalities. However, it is especially important for opioid treatment providers (OTPs) both because OTPs are subject to strict regulations that generally do not apply to other modalities, and because disruption in patient access to medication leads to withdrawal and possible drug use relapse. This study surveyed OTPs in an area subject to seasonal hurricanes to examine the effects hurricanes and other disasters on them and the measures taken to mitigate their impact.

**Methods:** A 30-minute self-administered survey was distributed to OTP program directors in the five Gulf Coast states: Alabama, Florida, Louisiana, Mississippi, and Texas. A sampling frame of 141 OTPs was compiled from lists of providers maintained by regulatory authorities. The response rate was 63.1% (89 of 141).

**Results:** Data indicate 47.6% OTPs have experienced structural or infrastructural problems due to hurricanes and 46.3% have had such problems due to other disasters. 75.6% have experienced service delivery problems due to hurricanes and 17.1% have had such problems due to other disasters. Most common structural/infrastructural problems are loss of electricity, disrupted telephone and internet, and transportation problems. Most common service delivery problems are influx of displaced patients, inability to verify dosage of displaced patients, extended hours, and staff shortages.

98.7% have a disaster plan and 71.4% have MOU with another agency for back-up dosing. 87% conduct mock runs of their plan, but only 15.9% have partnered with another agency in an exercise. 54.6% store client data off-site. Only 36.4% thought it likely they would get help from local agencies in a disaster. For 55.8% OTPs the most common way staff update their knowledge about disaster planning is informal conversation. Only 28.1% are reimbursed for disaster planning.

**Conclusions:** Gulf Coast OTPs are vulnerable to hurricanes and other disasters. While most OTPs have a disaster plan, OTPs vary with respect to other mitigation measures.

**Support:** National Institute on Drug Abuse; Robert Wood Johnson Foundation

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**RELATIONSHIP BETWEEN THE SUBJECTIVE AND DISCRIMINATIVE EFFECTS OF D-AMPHETAMINE: A RETROSPECTIVE ANALYSIS.**Megan M Poole<sup>1,2</sup>, A R Reynolds<sup>1</sup>, A R Vansickel<sup>1,2</sup>, C R Rush<sup>2,1,3</sup>; <sup>1</sup>Psychology, University of Kentucky, Lexington, KY, <sup>2</sup>Behavioral Science, University of Kentucky, Lexington, KY, <sup>3</sup>Psychiatry, University of Kentucky, Lexington, KY

**Aims:** Drug discrimination is often used as an alternative to or in conjunction with subjective effects questionnaires in the assessment of the central effects of abused drugs. The purpose of this retrospective analysis was to further examine the relationship between the subjective and discriminative effects of d-amphetamine.

**Methods:** Twenty-seven human participants were included in the analyses. Participants in all studies learned to discriminate 15 mg d-amphetamine. After acquiring the discrimination (i.e. >80% correct responding on 4 consecutive sessions), the effects of a range of doses of d-amphetamine (0, 2.5, 5, 10, 15 mg) were tested. Outcome measures included responding on a drug discrimination task, subject-rated drug effect questionnaires, and cardiovascular indices. Data were analyzed with repeated measures ANOVA, planned comparisons, and simple regression.

**Results:** Results indicate that the discriminative and subjective effects of d-amphetamine were consistent with one another.

**Conclusions:** The results of this retrospective analysis could have important implications for the utility of drug-discrimination procedures for assessing the central effects of stimulants. Future studies should examine the relationship between subjective and discriminative effects using other classes of medications.

**Support:** Supported by NIDA DA010325, DA017711, and DA013567

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**TREATMENT OPTIONS FOR OPIATE DEPENDENCE: CHOICES BETWEEN BUPRENORPHINE AND METHADONE.**Michael R Polen<sup>1</sup>, D McCarty<sup>2</sup>, C Green<sup>1,2</sup>; <sup>1</sup>Center for Health Research, Kaiser Permanente, Portland, OR, <sup>2</sup>Public Health and Preventive Medicine, Oregon Health & Science University, Portland, OR

**Aims:** Methadone treatment has been the standard of care for individuals with opiate addictions. After FDA approval in 2002, buprenorphine emerged as an alternative pharmacotherapy. Clients and clinicians have begun to recognize advantages and disadvantages relative to methadone. It remains unclear, however, how physicians and patients choose between the two medications.

**Methods:** Using electronic databases from two non-profit health plans, we identified individuals with two or more prior-year diagnoses of opioid dependence. Semi-structured interviews with patients (n = 190) focused on addiction treatment experiences including use of and choice of medications. Qualitative analyses examined participants' comparisons of buprenorphine and methadone treatment experiences and choices made about medications.

**Results:** 20% of the sample reported prior treatment experiences with both buprenorphine and methadone; 25% reported experience with neither. Several themes emerged as important considerations for clients and clinicians when choosing between the two medications: 1) prior detoxification experiences with buprenorphine or methadone contribute strongly to decisions about current treatment, 2) perceived difficulty of withdrawal affects willingness to accept medications, particularly if the client's goal is to be drug free, 3) among clients with chronic pain, pain control is a strong influence on choice and 4) clients with chronic pain appear more willing to accept long-term maintenance medications if pain is controlled.

**Conclusions:** The emergence of buprenorphine as a viable pharmacotherapy for individuals with opiate dependence offers new opportunities for clients and clinicians to negotiate individualized treatment plans. Evidence from this study does not suggest that buprenorphine will—or should—replace methadone for treating opiate addiction. Rather, each medication continues to play a significant role, enhancing treatment options and patient choice.

**Support:** This research is supported by a grant from NIDA (R01 DA016341).

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**PSYCHOPATHY,VULNERABLE ATTACHMENT STYLES,DRUG ABUSE AND THEIR RELATIONS TO PATIENTS' OUTCOME IN METHADONE MAINTENANCE TREATMENT.**David Potik<sup>1,2</sup>, Y Abrams<sup>1</sup>, E Peles<sup>1</sup>, S Schreiber<sup>2,1</sup>, M Adelson<sup>1</sup>; <sup>1</sup>Dr. Miriam & Sheldon G. Adelson Clinic for Drug Abuse, Treatment and Research, Tel Aviv, Israel, <sup>2</sup>Psychiatry, Tel Aviv Sourasky Medical Center, Tel-Aviv, Israel

**Aims:** to evaluate the relation between different factors(factor 1-callous,remorseless use of others;factor 2-unstable lifestyle),vulnerable attachment styles,and their relation to drug abuse among former heroin addicts currently in MMT

**Methods:** 66 current MMT patients were studied between March 2007 and November 2008.The PCL-R, an instrument for the assessment of psychopathy,and the Vulnerable attachment style questionnaire which evaluates insecure,proximity-seeking,and overall vulnerable attachment style,were used.Drug abuse for opiates,cocaine,benzodiazepines,cannabis and amphetamines in month before filling the questioners was recorded,and defined as positive if any of the drugs was positive

**Results:** Fifty patients with insecure attachment style as compared to 16 patients with secure attachment style had higher factor 1(6.7±4 vs. 5.5±3.4,F=1.2,p=0.2),factor 2(10.7±4 vs. 8.8±4,F=2.4,p=0.1)and total score(19.7±8.1 vs. 16.5±7.8,F=1.8,p=0.1).Both factor 1 and 2 were significantly higher among drug abusers(n=35)compared with non drug abusers(n=31) factor 1(4.6± 2.9 vs. 8.5± 3.8; F=21.7,p<0.0005),factor 2(8.4± 4.1 vs. 12.5± 3.4; F=19.7,p<0.0005).

The 49 patients with vulnerable attachment style as compared to 17 patients with non vulnerable attachment style did not differ in factor 1,factor 2 and total score. But,examination of factor 2 facets showed that facet 4 (antisocial behavior)was higher among vulnerable vs. non vulnerable(5±2 vs. 3.6±2.4,F=5.6,p=0.02)and insecure vs. secure(5±2 vs. 3.4±2.3,F=6.8,p=0.01)but did not relate to drug abuse,while facet 3(impulsive lifestyle)was higher among drug abusers vs. non abusers(7.4±1.8, vs. 4.4±2.6, F=28,p=0.01)but was not related to vulnerable and insecure attachment styles

**Conclusions:** MMT Patients with high factor 2 scores are characterized with insecure and vulnerable attachment styles,and have chronically unstable and antisocial lifestyle which is characterized in drug abuse.

**Support:** Adelson Family Foundation



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# A SYSTEMATIC REVIEW OF GENDER DIFFERENCES IN HIV SEXUAL RISK BEHAVIORS AMONG STIMULANT AND OPIOID ABUSERS.

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**Aims:** Gender differences have been identified as a potential factor influencing the frequency and pattern of HIV sexual risk behaviors (SRB) among drug involved individuals. This systematic review documents gender differences in the prevalence and correlates of SRB among female and male stimulant and opioid abusers.

**Methods:** Electronic search of PubMed and PsycInfo databases for papers involving U.S. adults published from 1995 to 2008 yielded 924 articles. 398 were excluded because they presented only qualitative data, contained no original empirical data, or did not meet prespecified search criteria. Manual review of papers by the authors excluded additional papers. Reasons for exclusion included: gender data not provided (n=119) and single sex sample (n=223). This resulted in 34 studies reporting SRB frequencies by gender, and 64 studies reporting multivariate results including gender.

**Results:** SRB were studied in 30,231 males and 16,741 females. Eleven studies described gender differences as a primary focus of analysis. Study designs were primarily cross-sectional (n=31). Samples were drawn from community settings (n=23), substance abuse treatment programs (n=6), or a combination (n=5). Samples comprised of combined opioid and stimulant users were most common (n=20). Most commonly, SRB were reported as any sexual activity (yes/no), more than one sexual partner (yes/no), any sex trade (yes/no), and any unprotected sex (yes/no). Past 30 days was the most common time interval used to assess SRB. No clear patterns emerged with regard to gender differences.

**Conclusions:** Most studies examining SRB among opioid and stimulant abusers do not conduct gender analyses. Of those that do report gender differences, there is variability in how SRB is defined and the interval over which it is assessed. This makes it extremely challenging to evaluate whether gender SRB differences are present. Further research using improved methods is needed to examine whether gender differences are important in addressing SRB in substance abusing populations.

**Support:** DA022297 DA15831 DA022288

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# CONDUCT DISORDER PREDICTS EARLY BUT NOT LATE ONSET COCAINE USE AND DEPENDENCE: EVIDENCE FROM THE FAMILY STUDY OF COCAINE DEPENDENCE IN ST. LOUIS.

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**Aims:** The present study tests the hypothesis that Conduct Disorder (CD) predicts early (age 18-25) but not late (> age 25) onset cocaine use and dependence in a St. Louis community sample of 346 sibling pairs. We test the secondary hypothesis that late but not early onset use and dependence are associated with low educational attainment and unmarried status—characteristics that reflect difficulty meeting the developmental goals of emerging adulthood (Arnett, 2005). Finally, we examine the racial differences (Black vs. White) associated with early and late onset cocaine use and dependence and their risk factors.

**Methods:** General Estimating Equation (GEE; Hardin & Hilbe, 2003) models were used to perform multivariate analysis while controlling for sibling correlation and respondents' age. Chi-squares tests were used to describe racial differences in the prevalence of outcomes and their risk factors.

**Results:** 24% (N=163) of subjects endorsed early and 13% (N=87) late onset cocaine use. 12% (N=80) met the criteria for lifetime dependence with early onset use, and 7% (N=50) met the criteria with late onset use.

As hypothesized, the presence of CD predicted early onset cocaine use (OR=2.92, p<.001) and dependence (OR=3.69, p<.001) but not late onset use or dependence. Low educational attainment predicted late but not early onset use (OR=3.56, p<.01) and dependence (OR: 5.13, p<.01). Unmarried status predicted late but not early onset use (OR: 2.17, p<.05). There were significant racial differences in the distribution of the outcomes and their risk factors.

**Conclusions:** Cocaine use and dependence are heterogeneous health problems. When they emerge in early adulthood, they are often associated with behavioral problems that began in childhood. When they arise in middle adulthood or later, they are more often associated with difficulty meeting the developmental challenges of emerging adulthood. Race is associated with differential risk for and development of cocaine use and dependence across the lifespan.

**Support:** Supported by NIH R01 DA 13423 and 19963.

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# STRENGTHS-BASED CASE MANAGEMENT FOR DRUG-ABUSING PAROLEES: OUTCOMES AT THREE AND NINE MONTHS USING TWO CAUSAL MODELS.

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**Aims:** An obstacle to the effectiveness of community substance abuse treatment for parolees is low treatment engagement—the failure of parolees to show up for scheduled treatment and their tendency to drop out early. To address this re-entry problem, the Transitional Case Management (TCM) study, conducted under NIDA's Criminal Justice Drug Abuse Treatment Studies (CJ-DATS) cooperative, tested whether a strengths-based case management intervention would increase participation in community substance abuse treatment, enhance access to needed social services, and improve drug use and crime outcomes.

**Methods:** 812 inmates from four sites were randomly assigned to the TCM group or to a Standard Referral (SR) group. Using data from the three- and nine-month assessments (follow-up rates of 91% and 90%, respectively), the presentation will report results on whether parolees in the TCM group showed better outcomes than did parolees in the SR group with respect to treatment participation, number of other services received, drug use, and criminal justice involvement. The outcomes were assessed using two causal effects approaches: Intent-to-Treatment (ITT), which provides an unbiased estimate of the effect of randomization, and Complier Average Causal Effects (CACE), which estimates the treatment effect among participants who comply with treatment.

**Results:** In neither approach did the TCM group differ significantly from the SR group on the main outcomes of interest, overall or within specific sites.

**Conclusions:** The null results found in this study are discussed in terms of other research on case management for substance abuse clients and of their implications for using case management with substance-abusing parolees.

**Support:** NIDA grant U01DA16211

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# CRAVING AND USE OF TOBACCO AND COCAINE: FINDINGS FROM AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY WITH POLYDRUG USERS.

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**Aims:** To investigate how tobacco craving and use is related to cocaine craving and use through prospective real-time assessment in daily life in methadone-maintained outpatients who met DSM-IV criteria for heroin and cocaine dependence and were tobacco smokers.

**Methods:** For up to 20 weeks, 100 participants in methadone maintenance carried PalmPilots (PDAs) and self-reported on their mood, behaviors, and environment in 2-5 randomly prompted entries per day. Participants were also instructed to initiate a PDA entry whenever they craved or used cocaine or heroin (event-contingent entries). At each entry, participants reported whether they were smoking and rated tobacco and cocaine craving on 4-point scales. Smoking frequency was calculated separately for each of 4 levels of craving ratings in random-prompt (RP) entries and at event-contingent (EC) entries involving cocaine craving or cocaine use. Data were analyzed by repeated-measures logistic regressions (SAS GLIMMIX macro).

**Results:** Smoking frequency increased linearly with RP ratings of tobacco craving ( $F(1,272) = 117.34, p < .0001$ ) and cocaine craving ( $F(1,246) = 82.06, p < .0001$ ).

Smoking frequency was similar during EC episodes of cocaine use (54%), cocaine craving (51%), and RP reports of high cocaine craving (50%). Smoking frequency was significantly lower during RP reports of low cocaine craving (29%). Significant differences in smoking frequency (Tukey-Kramer  $p < .001$ ) were found between RP reports of Low vs. High Craving, RP reports of Low Craving vs. EC reports of cocaine craving, and RP reports of Low Craving vs. EC reports of cocaine use.

**Conclusions:** Tobacco use and craving were strongly associated, with rates of smoking highest when tobacco craving was highest. Tobacco smoking was also strongly associated with cocaine craving and use. These results are consistent with previous research suggesting a link between nicotine and cocaine addiction and may have implications for treatment.

**Support:** NIH National Institute on Drug Abuse Intramural Research Program

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**GENDER DIFFERENCES IN RESPONSE TO MARIJUANA CUES AND STRESS IN MARIJUANA-DEPENDENT INDIVIDUALS.**

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**Aims:** Drug-related cues and stress have been identified as predictors of relapse in other drug dependencies, but little research on the contribution of these factors to marijuana use exists. The influence of gender on these factors has also been explored, but not in marijuana-dependent individuals. This laboratory-based study was conducted to explore the influence of gender and stress on reactivity to marijuana cues in marijuana-dependent individuals.

**Methods:** In this investigation, HPA axis (e.g., ACTH, cortisol) and physiological (systolic and diastolic BP) responses to the presentation of marijuana cues were assessed in male and female marijuana-dependent individuals after randomization to a psychological stressor (Trier Social Stress Task; TSST) or no-stress control condition. Subjects were between the ages of 18 and 65 years who met DSM-IV criteria for marijuana. Blood draws were performed 8 times for the neuroendocrine measures and physiological measures were collected 6 times over the 2-h protocol. Area under the curve (AUC) and maximum response (MAX) was constructed for each variable. The Mann-Whitney test was performed to examine gender differences within the stress and no-stress groups exposed to marijuana cues.

**Results:** Groups assigned to the no-stress condition had no gender differences in neuroendocrine or physiological response to the cues. However, in the groups that were additionally exposed to the TRIER, males displayed greater cortisol responses (AUC,  $p=.005$ ; MAX,  $p=.023$ ) than did the females, although gender differences in ACTH levels did not reach statistical significance. In addition, males displayed higher systolic (AUC,  $p<.001$ ; MAX,  $p<.001$ ) and diastolic (AUC,  $p=.038$ ; MAX,  $p=.048$ ) blood pressure responses during the procedure.

**Conclusions:** While there do not appear to be gender differences in neuroendocrine or physiological response to marijuana cues, marijuana-dependent females display a blunted response to a psychological stressor compared to males. **Support:** Supported by NIDA grants R21DA022424 (McRae-Clark) and K24DA00435 (Brady)

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**ASSESSING PARTICIPATION IN A RANDOMIZED TRIAL EVALUATING IMPROVEMENT STRATEGIES IN ADDICTION TREATMENT.**

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**Aims:** This research aims to assess participation in a national multi-center randomized trial. It is hypothesized that differences in agency participation may be attributable to the state in which research is conducted, intervention arm assigned, and provider organizational characteristics related to change readiness.

**Methods:** Participation statistics were calculated for the first cohort, representing 121 providers in three states, using meeting registration lists, teleconference roll calls, and electronic records of consultation calls. Participation hours were divided by the prescribed dose of intervention hours per arm to determine a 12-month participation rate for each agency. Univariate analysis of variance was conducted with participation rate as the dependent variable. The predictor variables were state, arm, and 28 dimensions of provider change readiness as measured by 859 provider survey responses. Results were deemed significant for  $p<.01$ .

**Results:** Intervention arm ( $p=.008$ ) and state ( $p=.001$ ) were both significant predictors of participation. Of the 28 dimensions of organizational readiness for change, two factors were significant: Management Staff Involvement in Change ( $p=.000$ ) was positively associated with participation while Support Staff Involvement in Change ( $p=.007$ ) was negatively associated with participation.

**Conclusions:** Organizational research setting may have an impact on participation. The perceived efficacy and mode of communication associated with each intervention arm may impact participation. Commitment to change by provider leadership is an important predictor of participation, and should be assessed when selecting organizations to participate in research projects. One unexpected finding was that Support Staff Involvement in Change was negatively associated with participation. This could be the result of factor collinearity and warrants further investigation.

**Support:** National Institute on Drug Abuse (5 R01 DA020832-02).

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**EDUCATING ADDICTION PROVIDERS TO USE THE NIATX PROCESS IMPROVEMENT MODEL TO ENHANCE CLIENT SERVICES.**

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**Aims:** Develop a framework for educating addiction treatment providers to use the NIATx model of process improvement (PI) to enhance client services. **Inquiry:** (1) What educational experiences best prepare staff to successfully use NIATx methods? (2) What sequence of learning experiences supports understanding, mastery, and a capacity to use and sustain the PI model?

**Methods:** Four core faculty members used an experiential adult learning model to create three progressive learning sessions. The framework included objectives to guide each learning session: (1) "Beginning and Learning" about the NIATx model (1 day), (2) "Using and Mastering" NIATx methods to make change (1.5 days), and (3) "Strengthening and Sustaining" changes and building a PI culture within their agency (1.5 days). State-level teams were consulted at each session. De-identified evaluations from participants were collected after each session to assess and further guide curriculum development.

**Results:** While participants generally believed that didactic learning experiences helped them to better understand the NIATx model, they also considered small group discussion and group work to be very helpful for learning PI methods. Participants and instructors noted that more than one day was needed to adequately cover an introduction to the NIATx PI model. The use of extensive participant discussion and guided project presentations were seen as very effective in helping agencies build the skills needed to use the NIATx model.

**Conclusions:** The progressive framework for guiding instruction was a key element in the design of an effective curriculum. Contributing strategies included: (a) using core faculty to establish a rapport and trust with participants, (b) collecting and incorporating de-identified evaluations from participants, and (c) effective communication with key stakeholders.

**Support:** Funded by the National Institute on Drug Abuse (5 R01 DA020832-02).

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**MALES, FEMALES, RECENT-ONSET DRUG DEPENDENCE, AND PSYCHOLOGICAL DISTRESS: EPIDEMIOLOGICAL EVIDENCE FROM THE UNITED STATES, 2006.**

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**Aims:** In this epidemiological research, we focus on the experience of a population sub-group with recent-onset illegal drug use but no recent tobacco or alcohol consumption, estimating male-female variations in their experiences of drug dependence and serious psychological distress (SPD).

**Methods:** In 2006, the US National Survey on Drug Use and Health (NSDUH) probability sample included 55,279 participants, ~10% of whom had started illegal drug use within 24 months of assessment (mainly cannabis smoking or prescription medicine misuse); 460 had consumed neither tobacco nor alcoholic beverages during the most recent 12-month assessment interval for which there was a multi-item assessment of clinical manifestations of DSM-IV drug dependence (CMDD); an NSDUH version of the K6 scale was used to assess serious psychological distress during the same 12 months. We used a generalized linear model and generalized estimating equations (GLM/GEE), with robust variance estimation to study variations in the CMDD experiences of drug users with and without SPD, with a focus on male-female differences after covariate adjustment for age, race-ethnicity, and self-assessed general health.

**Results:** Recent onset drug users with SPD were ~4 times more likely to have experienced CMDD than those without SPD (95% CI: 3.6, 4.6;  $p<0.05$ ). There was just one statistically robust sign of male-female variation: as compared to male counterparts, females with recent-onset illegal drug use and with SPD were more likely to have developed tolerance ( $p<0.05$ ).

**Conclusions:** These findings support prior clinical reports on sex related differences in both distress level and CMDD, which in turn should be expected to affect treatment seeking, course, and prognosis. Longitudinal research will be needed to disentangle various facets of the SPD-CMDD relationships, the temporal sequencing, and whether the SPD is attributable to the illegal drug use, or vice versa.

**Support:** R01DA016558, K05DA015799, MSU VPRGS funds.

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### ADOLESCENT OUTPATIENT SUBSTANCE ABUSE TREATMENT: ARE MANUAL-GUIDED INTERVENTIONS SUPERIOR TO USUAL CARE?

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**Aims:** There is widespread agreement on the need to improve the effectiveness of substance abuse treatment services for adolescents, and the dissemination of standardized, evidence-based treatment interventions is one strategy for effecting such improvements. Testing whether these interventions actually improve upon "care as usual", however, is challenging due to the diversity of "usual care" offered across treatment programs and to differences in the types of clients these programs attract.

**Methods:** In this study, we compare substance use outcomes of adolescents treated in 8 outpatient programs: 4 community treatment centers presumed to be providing good care and 4 programs that were part of a randomized clinical trial offering manual-guided, research-based interventions. We use a nonparametric casemix adjustment technique to test whether otherwise similar youth would have had better outcomes at 3 or 6-months post-treatment entry if they had received one of the manual-guided, research-based therapies instead of the care they received at the community-based program.

**Results:** After casemix adjustment for more than 80 factors associated with patient placement criteria, there were no significant benefits of receiving manual-guided interventions at 3 or 6-months. However, three of the eight individual programs (1 of which was community treatment center) were found to yield, on average, better outcomes than other programs serving comparable clients.

**Conclusions:** These results indicate that while some adolescent substance abuse treatment programs appear to produce better results than others, adoption of manual-guided interventions may not be a distinguishing feature of the better performing programs. Implications for both practice and policy, including cost effectiveness, are discussed.

**Support:** National Institute on Drug Abuse Grants R01 DA017507-01 (Andrew R. Morral), DA016722 (Andrew R. Morral) and R01 DA015697-01 (Daniel F. McCaffrey).

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### CONTINGENCY MANAGEMENT REDUCES SUBSTANCE USE AND INCREASES HEALTHY BEHAVIORS AMONG HOMELESS, OUT-OF-TREATMENT MSM.

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**Aims:** Homeless, substance-abusing men who have sex with men (MSM) suffer high rates of HIV, exchange sex for money or drugs, and often do not seek treatment. This project adapted contingency management (CM) for homeless, out-of-treatment, substance-abusing MSM in a community-based HIV prevention setting to determine whether CM would reduce substance use and increase prosocial, healthy behaviors.

**Methods:** Participants (N=131) were randomized 1:1 to a CM or control condition for a 24-week intervention with follow-up assessments at 7-, 9-, and 12-months post randomization. Participants in the CM condition received points exchangeable for goods and services for performing prosocial, healthy behaviors including drug and alcohol abstinence. Analyses of the longitudinal outcomes were conducted using random effects regression models.

**Results:** Participants averaged 36.4 years (SD=8.7), reported a mean educational level of 12.4 years (SD=2.8), and were racially and ethnicity diverse with 53% Caucasian/white, 23% African American/black, 17% Hispanic/Latino and 7% mixed/other. Participants were severely impaired, with high rates of physical (62%) and sexual abuse (50%), prior suicide attempt (48%), recent psychological problems (77%), major depressive disorder (19%), current methamphetamine dependence (63%), and HIV (28%). On average, CM participants submitted 3.8 less stimulant-positive urine samples ( $p=.04$ ), performed 14.3 more health-promoting behaviors ( $p<.001$ ), and achieved 7.1 higher Treatment Effectiveness Score ( $p=.06$ ).

**Conclusions:** CM can be implemented successfully in existing community-based prevention programs and facilitate non-treatment seeking homeless MSM to reduce substance use and initiate behaviors that improve overall functioning. Analyses of follow-up data are ongoing and will be important to establishing whether the effects of CM are sustained beyond the intervention period.

**Support:** This study supported by NIDA grant #1 R01 DA 015990

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### ABUSE LIABILITY OF CHRONIC HYPNOTIC USE IN INSOMNIACS.

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**Aims:** Primary insomnia is considered a chronic disorder, but concerns about chronic hypnotic abuse remain. Short-term studies suggest that hypnotics have a low abuse liability, but no studies have assessed liability beyond 2 weeks. This study evaluated abuse liability in insomniacs using clinical doses of hypnotics nightly for 4 months.

**Methods:** Primary insomniacs (N=27), meeting DSM-IV criteria, without psychiatric diseases or a history of drug dependency and in good general health were recruited. Participants had no other primary sleep disorders and a sleep efficiency of <85% on a screening sleep recording. Randomly assigned participants received either nightly 10mg zolpidem or placebo double-blind for four consecutive months. In months 1 & 4, one week self-administration assessment occurred in the sleep laboratory. For the zolpidem group on sampling nights 1 & 2, color coded zolpidem (10 mg) or a placebo capsule was administered. The capsule colors and drug were administered in counter-balanced order. The following 5 nights, choice of either 1, 2, or 3 zolpidem (5mg each) or placebo capsules occurred depending on color-coded sampling night experiences.

**Results:** Subjects in the zolpidem group took zolpidem more often than placebo ( $\chi^2=12.1$ ;  $p=0.001$ ). The percentage of insomniacs in the zolpidem group choosing zolpidem over the 5 nights did not differ significantly from month 1 to month 4 (69% to 89%),  $\chi^2=0.841$ ;  $p=0.359$ . The percentage of available zolpidem capsules self-administered (1, 2, or 3 each night) by the zolpidem group did not differ significantly from self-administration of placebo capsules by the placebo group at month 1 (46% and 53%;  $\chi^2=0.107$ ;  $p=0.743$ ) or at month 4 (43% and 45%;  $\chi^2=0.841$ ;  $p=0.359$ ). On average the zolpidem group self-administered a 7.25 mg nightly dose in both month 1 and 4.

**Conclusions:** Nightly use of zolpidem by insomniacs for 4 months did not result in an increase in the number of zolpidem capsules self-administered over a 5-day test period in month 1 and month 4.

**Support:** NIDA, grant#: R01DA17355 awarded to Dr. Roehrs.

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### DETECTION AND QUANTIFICATION OF ENDOGENOUS ARGININE VASOPRESSIN IN BLOOD USING MASS SPECTROMETRY.

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**Aims:** Recent studies have implicated the vasopressinergic system in drug abuse. It has a role in withdrawal-induced anxiety, as well as stress-induced reinstatement in rodent models of cocaine addiction. To aid in our investigations of the effects that drugs of abuse have on the vasopressinergic system we have developed novel methodology to unambiguously detect arginine vasopressin (AVP) in plasma and tissue of rats, using capillary liquid chromatography coupled to electrospray ionization tandem mass spectrometry (LC-MS<sup>2</sup>).

**Methods:** Rat plasma, prepared from trunk blood was obtained following euthanasia. Plasma samples were acidified and centrifuged through 10 kDa size exclusion filters; the filtrate was analyzed via LC-MS<sup>2</sup>. MS<sup>2</sup> generated fragment ions were used for the detection of AVP. Using a heavy-isotope labeled internal standard, <sup>13</sup>C<sub>5</sub>, <sup>15</sup>N-6-Pro-AVP, we were able to accurately quantify the levels of AVP using MS<sup>2</sup>.

**Results:** Our initial study compared AVP from Fischer and Lewis strains of rats, using our novel LC-MS<sup>2</sup> method. Our mass spectrometric findings are in accord to that reported in the literature for plasma AVP levels (less than 10 pM for both strains). During these studies, we found that a common method for rodent euthanasia, using carbon dioxide, leads to dramatic (more than 20-fold) and very rapid increases in plasma levels of AVP. These findings were compared with a widely-used radioimmunoassay method that was originally validated using a chromatographic approach.

**Conclusions:** Our LC-MS<sup>2</sup> method for the detection and quantification of AVP is comparable to RIA in sensitivity, and superior in specificity. This method will be valuable in investigations of the effects of drugs of abuse, including cocaine, alcohol, and heroin, on this and other neuropeptide systems, and was useful in discovering the unexpected effects of CO<sub>2</sub> on plasma AVP levels.

**Support:** NIH-NIDA Grant P60-DA05130 (M.J.K.), NIH-NCRR grant RR00862 (B.T.C.)

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# THE EFFECTS OF PROGESTERONE PRETREATMENT ON THE RESPONSE TO ORAL D-AMPHETAMINE: IMPULSIVITY, MOOD AND PERFORMANCE.

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**Aims:** Administration of progesterone during the follicular phase of the menstrual cycle in women who use cocaine has been shown to attenuate the positive subjective effects of cocaine. Thus, it was of interest to determine whether progesterone would alter the effects of d-amphetamine in normal healthy control women.

**Methods:** Eleven women completed six outpatient sessions over two menstrual cycles. During the follicular phase of each cycle, women were administered oral d-amphetamine (0, 10, 20 mg). Women were pretreated with oral micronized progesterone (200 mg) during the follicular phase of one cycle, and, during another cycle, women were pretreated with placebo progesterone. During each session, participants completed a range of tasks including subjective measures of abuse liability, cognitive performance tasks, and behavioral measures of impulsivity and risk-taking. These measures were assessed at baseline and several times after drug administration.

**Results:** Progesterone levels were significantly higher after oral progesterone administration compared to placebo progesterone administration. d-Amphetamine dose-dependently increased blood pressure and ratings of "Drug Liking" and this was not altered by progesterone pretreatment. There was no effect of d-amphetamine on heart rate or peak Stimulation or Sedation scores alone or in combination with progesterone. Peak performance on a motor coordination task and the Digit Symbol Substitution task also was not altered by d-amphetamine alone or in combination with progesterone. Four behavioral tasks were used to measure different components of impulsivity: the Immediate Memory Task, a GoStop task, a Delayed Discounting Task and the Balloon Analogue Risk Task. There were no effects of d-amphetamine alone or in combination with progesterone on any of the impulsivity measures.

**Conclusions:** These results suggest that d-amphetamine, progesterone, or the combination does not alter performance or impulsivity in normal healthy women.

**Support:** Supported by NIDA grant DA009114 (SME).

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# VALPROATE TREATMENT ENHANCES CUE-INDUCED COCAINE CRAVING.

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**Aims:** Based on prior clinical trials indicating that anticonvulsant medications reduce drug craving in cocaine dependent patients, we tested the effects of valproate treatment on cue-induced cocaine craving.

**Methods:** Crack cocaine dependent patients (N=20) were tested in a placebo-controlled, within-subjects, crossover study design. Valproate treatment was titrated up to 1500 mg/day by Day 6 of treatment, cue testing was completed on Day 8 of treatment, and all study participants underwent a washout period of 5 days between active and placebo medication treatment periods. Testing included both cocaine and neutral cue exposure sessions, presented in a random and counterbalanced order. Results were analyzed by ANOVA

**Results:** Main effects of cue exposure were found for subjective ratings of desire to use cocaine now, the cocaine craving index, cocaine-like high, and cocaine withdrawal. Treatment interaction effects were found with desire to use cocaine now, which was higher in the valproate condition. Main effects of medication treatment were found, in which lower blood pressure and heart rate, and higher plasma cortisol levels, were associated with valproate treatment. Valproate treatment was also associated, at a trend level, with higher pre-test cocaine craving levels.

**Conclusions:** These results demonstrate that cocaine cue reactivity is a robust phenomena across two assessment sessions, but fail to support the use of valproate as a means of reducing spontaneous and cue-induced cocaine craving

**Support:** NIDA DA12277 and NIDA DA017556

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# TRANSFER OF EXTINCTION LEARNING FOR THE CONDITIONED STIMULUS OF NICOTINE BY NICOTINIC RECEPTOR AGONISTS.

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**Aims:** Nicotine (NIC) functions as a conditional stimulus (CS) for a sucrose unconditioned stimulus (US). In this research, rats are given an injection of either NIC or saline before placement in a conditioning chamber. On NIC sessions, sucrose is delivered intermittently; on saline sessions, no sucrose is delivered. Conditioning is evidenced by an increase in head entries into the sucrose receptacle before a delivery on NIC sessions. Recently, we have identified several nicotinic acetylcholine receptor agonists that substitute for the NIC CS. This study determined whether these ligands would substitute for NIC during extended extinction training and to test for transfer of extinction learning.

**Methods:** To this end, in three separate experiments we tested 1) ABT-418 at 0.6 and 1 mg/kg, 2) varenicline at 0.1 and 3 mg/kg, or 3) nornicotine at 3 and 6 mg/kg. In these experiments, 0.4 mg/kg NIC was first trained as a CS. Rats were then assigned to groups during extinction that received NIC, saline, or one of two drug dose that either partially or fully substituted for NIC. Extinction training lasted for 6 consecutive daily 20-min sessions. For the transfer test, all rats were administered 0.4 mg/kg NIC and sucrose was withheld for the 20-min session.

**Results:** ABT-418 did not substitute for NIC during extinction or on the transfer test. In contrast, during extinction conditioned responding for 0.1 mg/kg varenicline and 3 mg/kg nornicotine was greater than saline and less than nicotine indicating partial substitution across repeated extinction sessions. This substitution transferred back to the NIC CS. Specifically, responding for the 3 mg/kg nornicotine group was significantly below saline and not different than NIC indicating full transfer of extinction learning to NIC. Responding in the 0.1 mg/kg varenicline group was intermediate to both NIC and saline indicating partial transfer.

**Conclusions:** These findings indicate that NIC evoked conditioned responding can be weakened by repeated non-reinforced presentations of an alternative drug that shares stimulus properties of NIC.

**Support:** DA018114 DA023283

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# DEVELOPMENT OF A PLATE ASSAY TO IMMUNO-HISTOCHEMICALLY DETECT BRAIN PROTEINS IN RECEPTOR AND SIGNALING PATHWAYS ASSOCIATED WITH ADDICTION.

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**Aims:** We have employed a 96-well plate assay to detect changes in the abundance of the 5-HT2C R, MEK and phosphorylated ERK (pERK) in adherent cultured cells expressing 5-HT2C R. We have shown that this assay is highly reliable, reproducible and amenable to assaying multiple conditions in the same experiment. Optimizing this plate assay for brain tissue presents the challenge of immobilization of the proteins in the wells. We chose several chemical modifications (epoxide glues, poly-d-lysine and paraformaldehyde) to aid in immobilization of tissue samples in the wells.

**Methods:** Plates were coated with poly-d-lysine, super glue, paraformaldehyde or poly-d-lysine/paraformaldehyde. Protein concentrations of crude rat brain homogenates were determined by the BCA assay. Protein was added to each well and the plates were centrifuged. To detect remaining protein, crystal violet was added to washed plates. Plates were washed to remove the crystal violet, and dried overnight at room temperature. Dye was extracted from each well with acetic acid and absorbance was read at 509 nm.

**Results:** Coatings except super glue immobilized proteins with various efficiencies. Increased immobilization was dependent upon protein content when assayed in poly-d-lysine and paraformaldehyde coated wells; the combination of the poly-d-lysine/paraformaldehyde resulted in the most significant amount of protein immobilization.

**Conclusions:** Poly-d-lysine, paraformaldehyde and the combination serve as efficient methods to immobilize proteins in 96-well plates. Experiments are underway to determine changes in 5-HT2CR, MEK and pERK in tissue dissected from rats withdrawn from cocaine after self-administration. These methods will provide a precise, more rapid means to assay multiple, key proteins in brain tissue in animal models of addictive processes.

**Support:** Grant support: NIDA grants DA022506, DA006511, DA020087

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**COMPARATIVE PHARMACOLOGY OF DEXTROMETHORPHAN AND TRIAZOLAM.**

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**Aims:** Dextromethorphan (DXM) is a widely used over-the-counter cough suppressant that is sometimes abused at high doses. The aim of this ongoing study is to characterize the clinical pharmacology of supratherapeutic doses of DXM in comparison to triazolam on various physiological, psychomotor, subjective, and cognitive measures.

**Methods:** Participants in this study have histories of nonmedical drug use including classic serotonergically mediated hallucinogens (e.g. psilocybin and LSD). Single, acute, oral doses of DXM (100, 200, 300, 400, 500, 600, 700, 800 mg/70 kg), triazolam (0.25, 0.5 mg/70 kg) and placebo are being administered under double-blind conditions using an ascending dose run-up design. Psychomotor, physiological, subject-rated, and cognitive effects are being assessed repeatedly after drug administration.

**Results:** DXM produced psychedelic-like effects in the first six subjects in this study. Triazolam produced dose-related sedation and psychomotor impairment but did not reliably increase most measures on the Hallucinogen Rating Scale (HRS). In contrast, DXM generally produced dose-related increases on five of six subscales of the HRS, reflecting changes in affect, perception, and cognition similar to those produced by classic psychedelic drugs. Four of six volunteers vomited after one or more doses of DXM above 300 mg/70kg. All drug effects resolved without significant adverse effects. In a follow up interview, the experience was described as personally meaningful with four of the six volunteers rating the experience as "among the 5 most spiritually significant experiences of my life".

**Conclusions:** High doses of DXM may produce effects with similarities to classic hallucinogens that are distinct from the sedative hypnotic triazolam.

**Support:** NIDA grant DA003889

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**THE IMPACT OF PAROLE OFFICER-OFFENDER RELATIONSHIPS ON RECIDIVISM AND SUBSTANCE USE: RESULTS FROM A RANDOMIZED TRIAL.**

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**Aims:** This study uses data from a randomized trial of offenders, Step'N Out, that tested a collaborative behavioral management (CBM) system in parole offices at 6 sites, to determine if CBM influenced the relationship between the parole officer and offender and whether this relationship impacted outcomes of drug use and arrest over the 9 month follow up period. The influence of other types of informal social bonds including employment and family and peer relations was also tested.

**Methods:** A total of 363 subjects were used in the analysis. Data from the PO-probationer relationships form was used to determine the quality of the officer-offender relationship. The outcome data was aggregated from the timeline follow back for the 9 month follow up period. Multi-level models were built, nesting monthly outcomes within persons and controlling for initial recidivism risk and substance dependency.

**Results:** Those in the CBM group had higher scores on the PO-probationer scale than those in the control group (means, CBM: 252.7, CTRL: 227.7;  $F=19.02$ ,  $p < .001$ ) and this applied across all subscales. In the regression models, the PO-probationer score was related to lower arrest rates and drug use over the 9 months of follow up. Employment at 3 months was related to lower drug use but not arrest rates.

**Conclusions:** The CBM intervention increased the quality of the officer-offender relationship compared to usual parole. This enhanced relationship appears to have a positive effect on offender recovery during the re-entry period. A two-pronged approach to revamping the current parole system is called for: to give parole officers the training to learn to engage the offenders in collaborative processes and to reduce caseloads of parole officers to reasonable numbers so that they can feasibly implement the CBM principles.

**Support:** This study was funded under Criminal Justice Drug Abuse Treatment Studies (CJ-DATS), a cooperative agreement from the National Institute on Drug Abuse.

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**EXAMINATION OF SOCIAL CONTEXTUAL VARIABLES AS RISK FACTORS IN THE RELATIONSHIP BETWEEN GENDER AND CRACK/COCAINE.**

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**Aims:** Among urban samples females have evidenced greater crack use compared to males. This is concerning because crack has been associated with a number of serious health-compromising behaviors. Study aimed to replicate previous findings indicating that females evidence greater frequency of crack use and to extend previous work by examining social contextual variables (use by others in their social network and means of obtaining) as risk factors.

**Methods:** Sample included 142 drug users who had used crack at least once in the past year and were currently enrolled in residential substance abuse treatment.

**Results:** As expected, females used crack significantly more frequently in the past year than males ( $F = 4.24$ ,  $p < .05$ ). For use, females reported more frequent use of crack by their romantic partner and family than did males ( $F = 3.55$ ,  $p < .05$ ). Further, use by romantic partner served as a significant risk factor in the relationship between gender and crack use frequency (Sobel  $z = 9.37$ ,  $p < .001$ ). Males and females did not differ across use by other categories of individuals (e.g., friends, people in their neighborhood). Regarding means of obtaining, females reported greater frequency of sex exchange ( $F = 19.45$ ,  $p < .001$ ) and receiving crack for free ( $F = 11.13$ ,  $p < .01$ ). Males reported a greater frequency of obtaining crack through money earned from dealing drugs ( $F = 6.83$ ,  $p = .01$ ). However, because these variables were not related to frequency of crack use, none served as a risk factor in the relationship between gender and crack use frequency.

**Conclusions:** This study adds to previous reports of greater crack use among urban females and identified frequency of use by romantic partner as a potential factor underlying greater use by females. Although not identified as risk factors in the relationship between gender and crack use, means of obtaining appear to differ by gender and may be an important determinant of HIV-risk behavior.

**Support:** NIDA 1 F31 DA023302-01A1 (PI: Reynolds) and NIDA R01 DA19405 (PI: Lejuez)

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**NEGATIVE AFFECT INTERACTS WITH IMPULSIVITY TO PREDICT DISTRESS TOLERANCE IN A SAMPLE OF INNER-CITY SUBSTANCE USERS.**

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**Aims:** Negative reinforcement processes emphasize that the motivational basis of addictive drug use is the reduction or avoidance of negative internal states. Research examining behavioral assessments of distress tolerance (DT), defined as the ability to persist in goal directed behavior in the face of affective distress, has provided support for negative reinforcement processes in substance use outcomes, such that low DT is associated with shorter abstinence and increased risk of treatment dropout among substance users. Although the negative outcomes associated with DT are well established, the mechanisms underlying DT remain unclear. One mechanism of interest is impulsivity (Imp). Recent evidence suggests that impulsive behaviors often occur in the presence of negative affect (NA). Thus, highly impulsive individuals may engage in negative reinforcement behaviors in the presence of NA as a means of regulating their emotions. Despite the theoretical link, empirical evidence of this association is absent from the literature. Thus, the aim of the current study was to test the extent to which DT is associated with Imp and NA in a sample of 132 inner-city substance users in residential treatment.

**Methods:** Participants completed two computerized tasks (PASAT & MT), with DT measured in latency in seconds to task termination. They also completed a self report (Barratt Imp Scale) and a behavioral measure of Imp (Delayed Discounting), as well as self reported NA before and after each task.

**Results:** Linear regression analyses indicated that self reported NA following the MT interacted with total BIS ( $p=.006$ ) and with the BIS Non-Planning subscale ( $p=.002$ ) to predict DT on the MT, and NA following the PASAT interacted with DD to predict DT on the PASAT ( $p=.05$ ) such that the links between Imp and DT were only strong at highest levels of NA.

**Conclusions:** Taken together, findings suggest that individuals who experience heightened NA in the face of stress and who are high in trait Imp may be most vulnerable to negative reinforcement behaviors.

**Support:** NIDA R01 DA18647

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**ADOPTION OF MEDICATIONS IN SUBSTANCE ABUSE TREATMENT: ACCESS, INTEGRATION AND WORKFORCE DEVELOPMENT.**

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**Aims:** Despite evidence that medicated-assisted treatment (MAT) improves outcomes, adoption and diffusion of pharmacotherapies has been slow. In order to facilitate adoption of medications in substance abuse treatment, a clear understanding of the role of the state authority and the challenges providers face is warranted. This study documents MAT implementation efforts within SSAs in 2007 and 2008.

**Methods:** This study used a mixed-methods design with semi-structured interviews and brief surveys. Participants included SSA representatives from 50 states and the District of Columbia, and data collection was completed in 2007 and again in 2008.

**Results:** Publicly-funded medication assisted treatment is available: methadone (47 states), buprenorphine (45 states) and oral naltrexone (42 states). SSAs reported that access to medications is a priority ( $M=3.7$ ;  $SD=1.0$  on a 1 – 5 scale). Qualitative findings reveal barriers including a lack of financial resources, cost of medications, reimbursement complexities, and a lack of state funding to support increased use of medications that prevent widespread access to medications. Respondents noted that workforce and community ideology and attitudes about medications are also barriers to adoption. SSAs reported a lack of support from providers, very few doctors willing to provide medications, and shame from the public and patients about living in a community with a methadone clinic or being a client of such a clinic.

**Conclusions:** Accelerating the adoption of medications in substance abuse treatment requires changes in funding, state policy, provider organization, workforce development and shifts in service delivery patterns, documentation and provider attitudes and beliefs.

**Support:** This work was supported by the Robert Wood Johnson Foundation, Award #58839.

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**THE EFFECTS OF NICOTINE PREEXPOSURE DURING PERIADOLESCENCE ON THE AVERSIVE AND PHYSIOLOGICAL EFFECTS OF ALCOHOL IN ADULTHOOD.**

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**Aims:** Initiation of nicotine use is greater during adolescence than adulthood and often precedes the use of alcohol (EtOH). Since the aversive effects of a drug limit its abuse potential, the present study examined the impact of adolescent nicotine exposure on the aversive effects of EtOH in adulthood.

**Methods:** Male Sprague Dawley rats ( $n=64$ ) were given daily IP injections of saline (S) or 0.4 mg/kg nicotine (N) from postnatal day (PD) 34-43 (periadolescence). At PD90, EtOH's aversive effects were assessed using the conditioned taste aversion (CTA) design. On conditioning Day 1, 20-min access to 0.1% saccharin was paired with 1 of 4 doses of EtOH (0, 0.56, 1.0, 1.8 g/kg; 15% v/v) creating the following groups (S-0, N-0, S-0.56, N-0.56, S-1.0, N-1.0, S-1.8, N-1.8). On the following 3 days, animals received 20-min access to tap water (no injections). This cycle was repeated 4 times. Following the 4th cycle, animals were given a 2-bottle preference test and saccharin preference was calculated. This served as extinction day 1, and 2-bottle tests continued for 8 extinction trials. Hypothermia, BAC and locomotor activity were then independently assessed following an acute EtOH challenge.

**Results:** The 2(Preexposure)x 4(Conditioning)x 4(Trial) repeated measures ANOVA revealed that nicotine preexposure during adolescence significantly attenuated the acquisition of EtOH-induced CTAs at the 1.0 g/kg dose of EtOH ( $p < 0.05$ ). The 2 x 4 x 8(Extinction Trial) repeated measures ANOVA revealed that Group N-1.0 extinguished the EtOH-induced CTA faster than Group S-1.0 ( $p < 0.05$ ). Nicotine preexposure also attenuated the EtOH-induced (1.0 g/kg) hypothermic effect ( $p < 0.05$ ), but did not impact BAC. There was a trend towards a nicotine preexposure-induced reduction in the locomotor suppressing effects of EtOH.

**Conclusions:** Nicotine exposure during adolescence appears to reduce the aversive effects of EtOH in adulthood, increasing its overall reinforcing effects and possibly increasing the risk for abuse.

**Support:** Supported by a grant from the Mellon Foundation.

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**CROSSVALIDATION AND INTEGRATION OF FOUR MENTAL HEALTH SCREENERS USING ITEM RESPONSE THEORY.**

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**Aims:** The purpose of this study is to assess the relative and joint validity of four screening measures of internalizing mental disorders as applied to a substance abuse population. We examined whether selection of items across the screening instruments would result in a measure with improved psychometric properties and sensitivity with respect to diagnostic classification.

**Methods:** The four instruments are the Global Appraisal of Individual Needs—Short Screener (GSS), the Psychiatric subscale of the Addiction Severity Index (ASI), the Psychiatric Diagnosis Screening Questionnaire (PDSQ) and the K10. Each of these instruments was compared to the Structured Clinical Interview for DSM-IV TR Axis I Disorders (SCID). Instruments were analyzed using the one-parameter Item Response Theory (IRT) model. Instruments were analyzed to assess unidimensionality, existence of floor and ceiling effects, and differential item functioning on demographic and diagnostic factors.

**Results:** A total of 546 participants were recruited across three substance abuse treatment sites. The sample was approximately two-thirds male, 75% never married, and 25% having criminal justice involvement. With respect to any mood disorder, 43% met criteria for a mood disorder within the past month prior to assessment, and 62 percent met criteria for any mood disorder at some point during their lifetime.

**Conclusions:** Preliminary analyses indicated that each of the screening measures was sensitive to identifying major DSM Axis I disorders, and supported the use of IRT as a measurement validation tool.

**Support:** This project was supported by a research award from the Canadian Institutes for Health Research. Grant #119685.

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**WOMEN'S PERSPECTIVES ON SCREENING FOR ALCOHOL AND DRUG USE IN PRENATAL CARE.**

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**Aims:** Background: Screening for both alcohol and drug use in prenatal care is widely promoted. Published literature does not consider women's perspectives on screening nor the potential negative ramifications of screening.

**Aims:** Describe women's expectations of and experiences with having alcohol and/or drug use identified by prenatal care providers and the actions women take in light of these expectations.

**Methods:** 20 semi-structured interviews and 2 focus groups were conducted with a racially/ethnically diverse sample of low-income pregnant and parenting women using alcohol and/or drugs (primarily meth-using) in Contra Costa County, CA.

**Results:** Most women were averse to having drug use identified. They were not concerned with having alcohol use identified. Women expected that being identified as a pregnant drug user in prenatal care would lead to psychological, social, and legal consequences, including feelings of maternal failure, judgment by providers, reports to Child Protective Services (CPS), and loss of children. Women did not trust providers to protect them from these consequences. They took steps on their own to protect themselves. They avoided and emotionally disengaged from prenatal care, attempted to stop using substances that could be detected by urine tests before going to the doctor, and shared strategies within social networks of other drug users for getting the benefits of prenatal care while avoiding consequences.

**Conclusions:** Considerations of the public health impact of screening for drug use in prenatal care should take account of implications of women's physical avoidance of and emotional disengagement from prenatal care. Possible implications include direct effects of late, limited, and no prenatal care on pregnancy outcomes as well as missed opportunities for other health promoting interventions, including screening and brief interventions for alcohol.

**Support:** NIAAA T32 AA07240, March of Dimes Community Award

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**HEROIN PURCHASING IS INCOME, PRICE AND ARREST-RATE SENSITIVE.**

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**Aims:** Findings on drug price, competing purchases, and past 30-day income and consumption, established in a previous study, are replicated and extended. Participants were asked to indicate to what extent hypothetical environmental changes (described in separate scenarios) would alter their heroin purchasing behavior.

**Methods:** This study used a semi-structured interview method to assess behavioral economic drug demand in heroin dependent research volunteers.

**Results:** In the overall sample (n=109), participants report they would significantly ( $p<.005$ ) decrease their heroin daily purchasing amounts (DPA) from their past 30-day levels (mean=\$60/day) if: (1) they encountered a 33% decrease in income (DPA=\$34), (2) family/friends no longer paid their living expenses (DPA=\$32), or (3) they faced four-fold greater likelihood of police arrest at their purchasing location (DPA=\$42). Statistically significant gender differences were found such that males were more responsive than females to hypothetical scenarios of (1) 33% income reduction (DPAf = \$38, DPAm = \$32), and (2) to arrest-probability scenarios. Non-injection users reported significantly greater reduction in heroin purchasing than injectors (DPAi=\$25, DPAni=\$19) to 33% income reduction. Regression analyses for predicting measures of heroin purchasing indicated that: (1) income and dealer availability significantly predicted unit purchase amount; (2) purchase time, dealer availability and income significantly predicted number of purchases per week; and (3) unit cost and income significantly predicted number of bags consumed per day. Analysis of income quartiles reveals that higher income levels are related to increased purchase amounts of heroin among these daily users but unrelated to other drug use.

**Conclusions:** One policy implication of these data is that increases in arrest rates and reductions in income supplements must be dramatic to influence heroin purchases. Reactions to income and arrest changes may also vary between groups (e.g. gender).

**Support:** (Supported by NIH/NIDA R01 DA15462)

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**THE IMPACT OF A THREE-HOUR CURRICULUM INFUSION ON UNIVERSITY STUDENTS' KNOWLEDGE AND ATTITUDES ABOUT THE NEUROSCIENCE OF ADDICTION: RESULTS FROM THE TWO-YEAR NIDA ENTERS COLLEGE PROJECT.**

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**Aims:** 1) To evaluate the impact of infusing a 3-hour curriculum infusion package (CIP) based on the science of addiction research into existing pre-service helping profession courses on student knowledge and stigmatizing attitudes about individuals with substance use disorders (SUD); 2) To compare Year 1 and Year 2 study results.

**Methods:** Replicating the methods used during Year 1, two sections of an introductory course in each of three pre-professional disciplines (criminal justice, nursing, social work) were selected. One section served as the curriculum infusion (implementation) group (N = 151); the other as the control group (N = 179). Pre/post-test knowledge and attitude measures were developed based on curriculum objectives using multiple choice and 5-point Likert scale response options.

**Results:** The number of students who completed pre-post infusion measures totaled 240 during Year 1 and 226 during Year 2. Year 1 and Year 2 results suggest a significant increase in knowledge of addiction and a corresponding decrease in stigmatizing attitudes between 1) the implementation vs. non-implementation groups; and 2) the implementation group pretest vs. post-test measures (complete item level analyses will be presented).

**Conclusions:** Results lend support to the effectiveness of infusing a brief 3-hour research-based addiction curriculum into existing undergraduate courses, thereby increasing knowledge and reducing stigmatizing attitudes related to individuals with substance use disorders. Thus, the findings from this study could have long-term implications for preparing helping professionals to work with individuals with SUD.

**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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**ABSENCE OF REBOUND INSOMNIA FOLLOWING CHRONIC HYPNOTIC USE.**

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**Aims:** Few studies have assessed the risk of rebound insomnia, the worsening of insomnia following drug discontinuation, as a function of duration of use. In the withdrawal literature it is suggested that withdrawal occurs at therapeutic doses. This study is the first to repeatedly test for rebound insomnia with chronic nightly hypnotic use for 4 months.

**Methods:** Primary insomniacs (N=33), meeting DSM-IV criteria, a sleep efficiency of <85% on a screening sleep recording and in good general health were recruited. Randomly assigned participants received, double-blind, either 10mg zolpidem or placebo nightly for 4 consecutive months. On nights 1, 2 and 7 zolpidem efficacy was assessed and rebound insomnia on nights 8, 9, and 14 of month 1 and nights 1, 2, and 7 of month 4, with 8-hr sleep recordings. To test for rebound insomnia placebo was substituted for zolpidem in the zolpidem group. No night differences within the three assessments were observed and data presented are 3-night averages.

**Results:** Zolpidem produced a significant average increase relative to placebo in total sleep time (TST), 7.0 vs. 6.2 hrs, [F(1,26)=8.93;  $p=0.01$ ]. On the month 1 and 4 placebo substitutions, TST did not differ between zolpidem and placebo groups (6.5 vs. 6.3 hrs;  $p=0.515$ ) and (6.6 vs. 6.2 hrs;  $p=0.326$ ), respectively. Both sleep latency (SL) and min of wake after sleep onset (WASO) were improved by zolpidem SL:17.0 vs. 32.3 min, [F(1, 26)=6.288;  $p=0.019$ ] and WASO:48 vs. 90 min, [F(1,26)=8.163;  $p=0.008$ ]. On placebo substitutions these measures returned to placebo level in month 1 (SL:20.74 vs. 26.18 min, ( $p=0.379$ ) and (WASO:78 vs. 78.6 min, ( $p=0.892$ ) and in month 4 (SL:26.75 vs. 40.56 min,  $p=0.311$ ) (WASO:72 and 91 min, ( $p=0.278$ ). Month 1 and 4 substitution data did not differ in either group.

**Conclusions:** Zolpidem improved sleep initiation, maintenance and duration at month 1. At a therapeutic dose, 10mg did not produce rebound insomnia or increase its likelihood as a function of chronic nightly administration for 4 months.

**Support:** NIDA, grant#: R01DA17355 awarded to Dr. Roehrs.

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**VALIDATION OF A QUESTIONNAIRE FOR SUGAR ADDICTION.**

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**Aims:** To describe the validation process of the short version of a questionnaire for sugar addiction, originally comprised by 20 items.

**Methods:** The questionnaire was applied in a Brazilian convenience sample of 500 patients (67% female; mean age 37.6 years; 43% from clinics). An Exploratory and Confirmatory Factor Analysis of the instrument was conducted. A Rasch Model analysis was also used to check for unidimensionality, and examine the questionnaire's item distribution.

**Results:** The best fit model of the instrument has two hierarchical levels with one general factor (sugar dependence) and two specific factors (impaired control and hedonism) with an adequate fit (CFI=0.973 and RMR=0.005). The Cronbach's alpha of the general factor was 0.75 and the specific factors presented values of 0.67 and 0.66 respectively. Although the instrument has a hierarchical structure of two levels, it could be considered unidimensional by the following evidence: the general factor could explain 46% of the communality; all items had good adequacy to the Rasch Model, with reliability of 0.99, infit between 0.86 - 1.14 and outfit between 0.71 - 1.20.

**Conclusions:** This first version of the questionnaire has good psychometric properties, and could be an important tool to ascertain general sugar dependence.

**Support:** No Support

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**PARTICIPATION IN SUBSTANCE ABUSE CLINICAL TRIALS: COMPARING GENDER AND RACIAL/ETHNIC GROUPS.**

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**Aims:** The use of evidence-based treatments (treatments proved effective through controlled randomized clinical trials) has become the practice for substance abuse treatment programs. Randomized clinical trials provide a rigorous demonstration of effectiveness and should be used to guide policy makers and clinical programs in the adoption of evidence-based practices and treatments (EBP).

The National Institute on Drug Abuse Treatment Clinical Trials Network (CTN) serves as a vehicle for providing EBP for substance abuse programs. The CTN conducts pharmacological and behavioral clinical trials with individuals seeking treatment at community treatment programs around the nation. The interventions typically studied are efficacious drug addiction treatments that are being tested for effectiveness in "real life" settings.

**Conclusions:** CTN studies collect data for primary and secondary outcomes at baseline, during treatment and at follow-up sessions typically ranging from 3 to 12 months. Participation in all aspects of the study throughout the follow-up phase is crucial to collecting necessary data. NIH policy requires that women and minorities be included in clinical trials, and investigators are expected to analyze the data by gender and racial/ethnic groups.

To date, the CTN has conducted 23 clinical trials. A total of 9,681 participants have been randomized, of which 40% are women, 22% African American and 19% are Hispanics. The CTN tracks a number of variables critical to management and analysis of clinical trial data, including the availability of primary outcome measures, the rate of treatment exposure (sessions attended) and the proportion of follow-up assessments obtained. This poster provides data comparing gender and racial/ethnic groups with respect to four key variables: (1) CTN trial participation; (2) availability of primary outcome measures; (3) treatment exposure; and (4) follow-up assessments.

**Support:** National Institute on Drug Abuse

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**ASSIGNMENT OF INVOLUNTARY PAYEES IN A VOLUNTARY MONEY MANAGEMENT INTERVENTION.**Marc I Rosen<sup>1,2</sup>, K Ablondi<sup>1,2</sup>, A C Black<sup>1,2</sup>, B J Rounsaville<sup>1,2</sup>, R A Rosenheck<sup>2,1</sup>; <sup>1</sup>Psychiatry, Yale University School of Medicine, New Haven, CT, <sup>2</sup>Psychiatry, VA Connecticut Healthcare System, West Haven, CT

**Aims:** Considerable literature suggests that assignment of a payee (representative payee and/or conservator) to manage clients' finances is inconsistently implemented. This post-hoc analysis tested the hypothesis that clients receiving a money management-based intervention would be more likely to be assigned a payee than clients in a control condition.

**Methods:** To date, 80 clients at a community mental health center with histories of substance use and at least \$450 monthly income have been randomly assigned to nine months of treatment with ATM, a money management-based condition, or the control condition. Clients were asked one year later if a payee had been assigned and when available, qualitative data was collected concerning the process of payee assignment.

**Results:** Altogether, significantly more clients in ATM (9 of 42) were assigned payees than participants in the control condition (2 of 38; Chi-Square=4.6, p=.03). Pathways to payee assignment among ATM clients were a positive experience in ATM among 5, increased attention to finances by third parties among two, and psychiatric difficulties in two.

**Conclusions:** Assignment of payees appears to be influenced by whether clients are willing to be assigned one and whether third parties such as treating clinicians attend to their clients' money management needs.

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**COMORBID PATIENTS IMPROVE ON SUBSTANCE USE AND PSYCHOLOGICAL SYMPTOMS IN PSYCHIATRIC DAY TREATMENT.**A Rosenblum<sup>1</sup>, Stephen Magura<sup>2</sup>; <sup>1</sup>National Development and Research Institutes, New York, NY, <sup>2</sup>Western Michigan University, Kalamazoo, MI

**Aims:** To determine outcomes for drug-using vs. non-drug using patients in a psychiatric day treatment program.

**Methods:** New admissions (N=229) to a large urban continuing psychiatric day treatment program were recruited during 2003-2005. Confidential personal interviews were conducted including: Symptom Checklist-10 (SCL-10), Colorado Symptoms Index (CSI), Positive Affect (PA), Quality of Life (QoL), self-reported use of cocaine, opiates, marijuana and (meth)amphetamine in the past 30 days, and urinalysis for these drugs. Subjects positive by self-report or urinalysis were categorized as users of the drug. Six-month follow-up interviews and urinalysis were conducted (82% response). Significance was set at p<.05.

**Results:** Age (mean) 39 y; male 60%; black 42%; Hispanic 41%; white 18%; public assistance 69%; major depression 25%; bipolar, 13%; other mood 13%; schizoaffective 13%; schizophrenia 13%; psychotic NOS 7%; anxiety 3%; other 13%; any drugs 59%; cocaine 33%; marijuana 31%; opiates 19%; (meth)amphetamines 6%. For the frequent drugs, the percentage of patients positive at admission who remitted from drug use at six months after admission significantly exceeded the percentage negative at baseline who initiated drug use. These respective percents were 48% vs. 11% for cocaine, 58% vs. 9% for opiates & 35% vs. 17% for marijuana. Overall, there were significant decreases in symptoms on the SCL-10 and CSI and significant improvement on Quality of Life, with no change on PA. Drug users and non-drug users generally experienced similar amounts of decrease in psychological symptoms, but drug users did not improve on Quality of Life, whereas non-drug users did.

**Conclusions:** Psychiatric day treatment appears to benefit comorbid patients by reducing the net number of patients who actively use drugs over time and by decreasing psychological distress to about the same extent as for non-drug using patients. Although this program is not an integrated treatment model, it does provide group therapy and peer support groups that address comorbid disorders.

**Support:** NIDA R01DA015912.

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**CHANGES IN CIGARETTE USE AMONG COCAINE ABUSERS IN A PHARMACOLOGIC TREATMENT TRIAL.**Lindsay R Rothenberg<sup>2</sup>, D J Brooks<sup>2</sup>, D Feldman<sup>2</sup>, A Bisaga<sup>1,2</sup>, J Mariani<sup>1,2</sup>, F R Levin<sup>1,2</sup>; <sup>1</sup>Psychiatry, Columbia University, New York, NY, <sup>2</sup>Substance Abuse, New York State Psychiatric Institute, New York, NY

**Aims:** Treatment seeking cocaine users have high rates of comorbid nicotine dependence. A major concern in substance abuse treatment is that individuals will substitute one drug for another. This study examined cocaine dependent (CD) individuals in a 14-week medication based treatment program to determine: 1) Do smoking patterns change among smoking participants and 2) Do CD individuals who reduce cocaine use by  $\geq 50\%$  increase cigarette use?

**Methods:** All participants met DSM-IV criteria for Cocaine Dependence as determined by the SCID. Smoking groups were defined as chronic smokers (smoke 30/30 days), non-smokers, and non-daily smokers (mean of  $17 \pm 4$  days/month). For all analyses we compared the 4 weeks prior to admission to the last 4 weeks of study participation.

**Results:** The sample included 37 participants, 87% were male, 41% Caucasian, 33% Black, 18% Hispanic and 8% other. The mean age was  $42 \pm 8$  yrs. No significant demographic differences were found among the 3 groups. There was no significant time or group effects on changes in the amount (mean cigarettes smoked per day) or frequency (number of smoking days) of cigarette use. When comparing individuals who achieved a substantial reduction in cocaine use (defined as  $\geq 50\%$  reduction in number of days used and \$ spent) to those who did not, ANOVA tests were not significant for changes in smoking pattern (frequency ( $F = 1.15$  p=.29) or amount ( $F = .05$  p=.83)). However, since baseline frequency of cigarette use was found to be predictive of smoking frequency at the end of the trial, we adjusted for baseline use in a separate model. Linear regression revealed that those who achieved a  $\geq 50\%$  reduction in cocaine use had significantly fewer smoking days at the end of the study compared to those who did not substantially reduce cocaine use ( $F = 148.2$ , p<.001).

**Conclusions:** These results suggest that individuals who decrease cocaine use do not substitute with nicotine; instead they might show a decrease in number of smoking days.

**Support:** NIDA #R01DA022217



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### IDENTIFICATION OF "AGONIST" AND "ANTAGONIST" ALLOSTERIC MODULATORS OF AMPHETAMINE-INDUCED DOPAMINE RELEASE.

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**Aims:** Recent studies identified novel allosteric modulators of the dopamine transporter (DAT). Two of these compounds, N-(diphenylmethyl)-2-phenyl-4-quinazolinamine (SoRI-9804) and N-(2,2-diphenylethyl)-2-phenyl-4-quinazolinamine (SoRI-20040), were partial inhibitors of D-amphetamine-induced DAT-mediated release of [3H]MPP<sup>+</sup> from striatal synaptosomes ("DAergic release"). The present study extends these initial observations.

**Methods:** We conducted DAergic release assays, using rat brain caudate synaptosomes and either [3H]MPP<sup>+</sup> or [3H]DA, according to published methods.

**Results:** Both SoRI-9804 and SoRI-20040 partially inhibited D-amphetamine-induced DA release measured with either [3H]MPP<sup>+</sup> or [3H]DA in a dose-dependent manner. SoRI-20040 and SoRI-9804 also partially inhibited DAergic release stimulated by DA and (±)-3,4-Methylenedioxymphetamine, demonstrating that the observed partial inhibition is not specific for a particular DAT substrate. SoRI-9804 and SoRI-20040 did not attenuate D-amphetamine-induced release of [3H]5-HT from serotonergic terminals. SoRI-20041 did not alter D-amphetamine-induced DAergic release, but attenuated the effects of SoRI-20040 – an "antagonist-like" action. Kinetic experiments demonstrated that SoRI-9804, in contrast to cocaine, slowed D-amphetamine-induced release of [3H]MPP<sup>+</sup> from dopaminergic nerve terminals.

**Conclusions:** The two major findings of this paper are: 1) the identification of both "agonist" (SoRI-9804, SoRI-20040) and "antagonist" (SoRI-20041) allosteric modulators of D-amphetamine-induced DAT-mediated DA release, and 2) [3H]DA uptake and D-amphetamine-induced DAT-mediated efflux can be separately modulated. Such agents may have therapeutic potential for the treatment of stimulant addiction, parkinson's disease and other psychiatric disorders.

**Support:** This work was supported by the Intramural Research Program, National Institute on Drug Abuse, NIH, DHHS.

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### DOES PRIOR TRAUMA MODULATE LIMBIC BRAIN RESPONSE TO AVERSIVE CUES IN COCAINE-DEPENDENT PATIENTS?

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**Aims:** A particular vulnerability to stress in drug-addicted individuals is thought to contribute to chronic relapse to drug use. Hence, we hypothesized that drug-dependent individuals with a prior history of trauma may be more sensitive to stress-related stimuli.

**Methods:** Event-related Blood Oxygen-Level-Dependent (BOLD) fMRI at 3 Tesla was used to measure the brain response to randomly-presented brief (500 msec) aversive cues from the validated International Affective Picture System in 19 treatment-seeking male cocaine patients. Stimuli were presented in a "jittered" order to optimize sampling of the hemodynamic response function (HRF) and average inter-stimulus interval was 2 seconds. Data were realigned, smoothed, normalized and analyzed with SPM 2, using HRF as the basis function. Statistical parametric maps were thresholded at  $t=2.0$  for pre-planned subtraction contrasts, focusing on limbic regions of interest.

**Results:** Patient datasets were divided into two groups based on trauma history ("Prior Trauma",  $n=9$  vs. "No Prior Trauma",  $n=10$ ) using a screening question from the Addiction Severity Index. Individuals with a prior history of trauma had a striking limbic brain response (particularly in the amygdala;  $p < .001$  cluster-corrected;  $2 > t < 10$ ) to the visible aversive cues, as compared to individuals without prior trauma.

**Conclusions:** Our data provide the first evidence that a prior history of life trauma is associated with an increased brain response (mostly in limbic regions) to visible aversive cues in cocaine-dependent males. The brain response that we observed may be a potential predictor of vulnerability to stress-related relapse in those patients. Prospective studies will explore the ability of a medication to modulate the patients' limbic brain response to the aversive cues.

**Support:** NIDA T-32 Training Fellowship; NIDA RO1 DA-10241; NIDA P60-DA-05186, NIDA P-50-DA12756; VA VISN 4 MIRECC; Alexander Foundation

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### SOCIAL NETWORK FACTORS INFLUENCING RECENT HIV TESTING IN DRUG USERS.

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**Aims:** While injection drug use is driving the US HIV epidemic, non-injection drug use is also associated with an elevated HIV risk and is more common than injection drug use. Since HIV testing is associated with reduced disease transmission, the CDC recommends routine testing for drug users. We aim to identify social network factors associated with recent HIV testing in a drug using population in NYC.

**Methods:** This analysis used baseline data from a prospective cohort study that enrolled newly initiated IDUs (heroin/crack/cocaine injectors  $\leq 3$  years) and non-IDUs (never injected; used non-injection heroin/crack/cocaine  $\geq 1$  year) recruited using respondent driven sampling and targeted street outreach in high-risk NYC neighborhoods. Surveys assessed sexual and injecting practices in the past 6 months, HIV testing history, demographics, and social network variables. The analysis was restricted to HIV- and recent HIV+ (<6 months) drug users ( $N=299$ ). Factors associated with HIV testing in the past 6 months were evaluated using non-parametric t-tests and logistic regression.

**Results:** The sample was 14% IDU, 70% male, 36% Hispanic, 51% black, mean age=33 years, and 73% had a recent HIV test. After adjustment, high school education ( $AOR=1.97$ ;  $CI=1.11-3.50$ ), lifetime testing frequency ( $\geq 3$  times) ( $AOR=2.15$ ;  $CI=1.22-3.82$ ), and a greater proportion of high school-educated social network members ( $AOR=1.01$ ;  $CI=1.00-1.02$ ) were associated with a higher odds of recent HIV testing. A greater proportion of social network members to talk to about drug-related issues was associated with a lower odds of recent testing ( $AOR=.98$ ;  $CI=.97-.99$ ).

**Conclusions:** These data suggest that among these heavy drug users, higher education and more educated networks increase the odds of recent testing, but that having a supportive informational network related to drug use does not.

**Support:** More research is needed to characterize supportive drug-use networks (i.e. drug use/non-drug use relationships, HIV prevention knowledge, etc) so that HIV testing services can be specifically targeted. Identifying network factors unexplored in this study that influence HIV testing could further inform targeted social network-based programs.

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### EFFICACY OF THE MANUALIZED COGNITIVE-BEHAVORIAL TREATMENT PROGRAM CANDIS FOR CANNABIS USE DISORDERS.

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**Aims:** Cannabis is the most commonly used illicit drug worldwide. Until very recently systematic research on cannabis treatment programs was rare, especially in Europe. We investigated the efficacy of the multicomponent CANDIS-intervention that included motivational enhancement therapy, cognitive-behavioral therapy and psychosocial problem solving for adolescents and adults with cannabis use disorders (DSM-IV).

**Methods:** In a randomized controlled trial  $n=122$  subjects with cannabis abuse or dependence aged 16 to 44 years were randomly assigned to 1.) a Standardized Treatment (ST;  $n=51$ ), 2.) a Targeted Standardized Treatment (TST;  $n=39$ ) or 3.) a Delayed Treatment Control group (DTC;  $n=32$ ). For the purpose of this poster the two treatment variants were collapsed into one Active Treatment group (AT;  $n=90$ ). Cannabis use disorders were assessed with the composite international diagnostic interview (M-CIDI). Treatment consisted of 10 sessions manualized therapy, subjects in the DTC group started treatments after a waiting period of 8 weeks. Assessments were conducted at baseline, prior and post each therapy session, after treatment completion and at a 3-month and 6-month follow-up.

**Results:** 49% of beginners were completely abstinent, 54% of completers. The retention rate was 86%. In the DTC group the abstinence rate was significantly lower (13%,  $p < .0001$ ). Program effects were maintained over a 3-month (51%) and 6-month follow-up (45%) period. Subjects also improved significantly ( $p < .001$ ) in the frequency of cannabis use per week, addiction severity, number of disability days, and overall level of psychopathology.

**Conclusions:** The study demonstrated that CANDIS treatment is efficacious in obtaining abstinence and reducing the cannabis use, as well as in improving associated social and mental health burden.

**Support:** German Federal Ministry of Health, German Federal Ministry of Education and Research, Conducted in the framework of ASAT (Allocating Substance Abuse Treatments to Patient Heterogeneity) research network.

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**COCAINE CHOICE IN HUMANS DURING D-AMPHETAMINE MAINTENANCE.**

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**Aims:** Chronic treatment with agonist therapies like d-amphetamine attenuates the behavioral effects of cocaine in laboratory animals and in human volunteers. This study determined the effects of d-amphetamine maintenance on cocaine choice behavior in human volunteers. We predicted d-amphetamine maintenance would reduce cocaine choice.

**Methods:** Two d-amphetamine maintenance conditions were completed in counter-balanced order (0 and 40 mg/day). After 3-5 days of placebo or d-amphetamine maintenance, volunteers completed 5 experimental sessions. During these sessions, the volunteer first sampled placebo (i.e., 4 mg intranasal cocaine) identified as Drug A. Volunteers then sampled a second intranasal drug dose (4, 10, 20 or 30 mg cocaine) identified as Drug B. Volunteers then made 6 discrete choices between Drug A and Drug B. Drug choices were separated by 45 minutes. The primary outcome measure was choice differential (i.e., drug choices minus placebo choices). To determine whether outcomes varied by maintenance condition, orthogonal polynomials were used to partition the linear and quadratic components of the cocaine dose-response curves during placebo and d-amphetamine maintenance.

**Results:** Eight volunteers completed the study. During placebo maintenance, significant linear and quadratic trends were detected for cocaine choice. During d-amphetamine maintenance no such trends were observed. The absence of significant linear and quadratic trends during the active maintenance condition suggests that d-amphetamine attenuated the reinforcing effects of cocaine. Cocaine was well tolerated during d-amphetamine maintenance and no adverse events occurred.

**Conclusions:** These results are concordant with those of previous preclinical experiments, human laboratory studies and clinical trials that suggest agonist replacement therapy may be a viable strategy for managing cocaine abuse. Human laboratory studies can be used to screen putative pharmacotherapies prior to clinical trial testing.

**Support:** R01 DA021155

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**THE ACUTE SUBJECTIVE EFFECTS OF COMBINED BENZYLPIPERAZINE AND TRIFLUOROMETHYLPHENYLPIPERAZINE ON HEALTHY MALES.**

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**Aims:** The use of Benzylpiperazine (BZP) and trifluoromethylphenylpiperazine (TFMPP) has increased significantly in recent years as they have been exploited as legal alternatives to methylenedioxymethamphetamine (MDMA/Ecstasy) and other amphetamines. This double blinded, randomised study aimed to assess the acute subjective and physiological effects of these compounds in human males.

**Methods:** Healthy participants (age:22±3years) were given a single oral dose of placebo (n=16) or a combined dose of BZP and TFMPP (100mg,30mg respectively, n=20) and tested before and after drug administration. Subjective and mood effects were evaluated using the Profile of Mood States (POMS) questionnaire, Visual Analog Scales (VAS) and the Addiction Research Centre Inventory (ARCI). Blood pressure, body temperature and resting heart rate were measured at both time points.

**Results:** Combined BZP/TFMPP significantly increased systolic (Pre:127±11, Post:140±17mmHg) and diastolic (Pre:72±12, Post:81±11mmHg) blood pressure and heart rate (Pre:67±11, Post:77±13beats/min) compared to placebo. BZP/TFMPP significantly increased the VAS ratings of Stimulated and High. Significant effects were also observed in the categories of Good Drug Effect, Drug Liking and Bad Drug Effect. Combined BZP/TFMPP significantly decreased sedation and increased scores of energy, amphetamine-effects and dysphoria measured using the ARCI scales. Furthermore the POMS also demonstrated that BZP/TFMPP significantly decreased Fatigue.

**Conclusions:** The combination of BZP/TFMPP has produced different subjective mood ratings in comparison to the results found from previous trials in our laboratory after giving either BZP or TFMPP alone. In comparison, the effects of combined BZP/TFMPP on blood pressure and heart rate were similar to BZP and TFMPP when given alone dissociating the physiological and subjective effects. The results suggest combined BZP/TFMPP exert different neuropsychological effects in comparison to when taken alone.

**Support:** Trecia Wouldes

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**IMPACT OF RECENT DRUG USE ON THE VALIDATION OF SCREENING TOOLS FOR MENTAL DISORDERS.**

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**Aims:** Recent drug use is a concern in studies validating screening tools for mental disorders, given the potential for intoxication or withdrawal to influence item responses. Screening tools for mental disorders also need to perform well in situations where substance use is common. Using a sample drawn from a heterogeneous substance abuse treatment population, we examined the effect of past 24-hour substance use on the agreement between broad structured clinical interview for DSM-IV (SCID) diagnoses (any mood disorder and any internalizing disorder) and scores on four short screening tools: Psychiatric Diagnostic Screening Questionnaire, K10, GAIN-Short Screener and the psychiatric sub-scale of the ASI.

**Methods:** 546 clients were recruited from three large treatment centres in Ontario, Canada. Clients completed the screening tools and received an independent, same-day structured clinical interview (SCID). Since previous work showed high agreement with the self-report measures and urine testing, self-report was used to measure recent substance use. Performance of each measure against the gold standard SCID interview was examined using ROC analysis for four separate groups: No use (n=345); alcohol use only (n=41); alcohol and other drug use (n=91); and drug use without alcohol use (n=111).

**Results:** The ability of the screening tools to identify "any internalizing disorder" or "any mood disorder" was not compromised by substance use in the past 24 hours. For example, for the GAIN-SS, the AUCs for the four groups ranged from 0.74 to 0.79 and, for the PDSQ depression sub-scale, from 0.71 to 0.76.

**Conclusions:** Performance of the screening tools was robust with respect to recent drug or alcohol use. This supports the validity of results from our larger study of these short screening tools and suggests that such tools are not inappropriate in situations where substance use is common.

**Support:** This project was supported by a research award from the Canadian Institutes for Health Research: Grant #119685.

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**BUILDING MOMENTUM FOR IMPROVING CLIENT ENGAGEMENT AND RETENTION IN TREATMENT: THE CALIFORNIA EXPERIENCE.**

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**Aims:** Interest in the Network for the Improvement of Addiction Treatment (NIATx) model of process improvement is mounting in California. For the past four years, UCLA ISAP/the PSATTC has partnered with the NIATx National Program Office, CSAT, and several key California-based stakeholders to introduce process improvement in such a way that a broad and sustainable application of the NIATx model has emerged. This paper will present key findings from a phase II NIATx demonstration project with LA County-based treatment providers. The project utilized a peer learning collaborative model and offered a structured format for participants to learn about fundamental process improvement principles, tools, and techniques that could be used to prioritize ideas for change and implement improvement projects to impact treatment waiting time, no-shows, admissions, and continuation. A major emphasis throughout the project was the use of administrative data to track and measure the impact of rapid cycle change efforts. The collective knowledge and experience gained through the LA County pilot project has helped to inform a statewide roll-out of a training and technical assistance dissemination plan whereby treatment providers from throughout California have been oriented to process improvement and have been given opportunities for ongoing learning.

**Conclusions:** The paper will conclude with a discussion of a CSAT-funded demonstration project designed to increase NIATx coaching capacity in California, as well as a California Endowment-funded project to enhance ACTION Campaign recruitment and establish a series of five regional learning collaboratives throughout California.

**Support:** LA County ADPA, SAMHSA/CSAT, and the California Endowment

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**IDENTIFYING POOR PROGNOSIS PATIENTS IN COCAINE-ALCOHOL DEPENDENCE TREATMENT TRIALS.**

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**Aims:** Previous research has shown that urine drug screen results at baseline are a strong predictor of treatment outcome. Individuals who submit a cocaine-positive urine at baseline are less likely to achieve continuous abstinence and provide cocaine-negative urines during treatment. However, though it has been established that baseline urine results are predictive of treatment outcome, the variables associated with a cocaine-negative urine at baseline are less clear. We sought to determine what other pre-treatment variables were related to cocaine abstinence at the start of treatment.

**Methods:** Baseline urine drug screen results were obtained from 193 cocaine and alcohol dependent patients participating in an outpatient pharmacotherapy trial. The screening period of the study consisted of 6 visits over 2 weeks. Cocaine craving was measured weekly during screening using the Brief Substance Craving Scale (BSCS) and cocaine withdrawal severity was measured at each of the 6 screening visits using the Cocaine Selective Severity Assessment (CSSA). Pre-study Timeline Followback (TLFB) and Addiction Severity Index (ASI) data were also examined.

**Results:** Preliminary results show that high levels of cocaine craving and cocaine withdrawal symptoms at the start of screening were associated with a cocaine-positive urine at the start of treatment. Additionally, the number of days of cocaine and alcohol use in the 90 days prior to intake negatively correlated with the number of cocaine-negative urines submitted during the 6 screening visits. Demographic information collected on the ASI revealed that individuals who reported living with a drug user were less likely to submit a cocaine-negative urine at the start of the treatment phase.

**Conclusions:** Initial cocaine craving and withdrawal, the number of days of cocaine and alcohol use prior to treatment, and baseline reports of household drug use are all associated with urine drug screen results at the start of a pharmacotherapy trial.

**Support:** This work was supported by NIDA grant P50-DA-12756-02 to Helen Pettinati

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**MODIFIED THERAPEUTIC COMMUNITY FOR PERSONS WITH HIV/AIDS AND CO-OCCURRING DISORDERS.**

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**Aims:** This study focuses on the effectiveness of a Modified Therapeutic Community Aftercare (MTC-A) program for clients diagnosed with HIV/AIDS and co-occurring substance use and mental disorders.

**Methods:** Following residential MTC treatment, subjects entered either a MTC-A program (n=42) or a control condition (C; n=34), comprised of standard aftercare services. Interviews conducted at baseline (residential treatment entry) and at 6 months post residential treatment collected standard data to examine mental health, substance use, HIV-risk, and medication adherence.

A propensity model used to rebalance the sample, organized subjects into three strata. Subjects in the High stratum reported greater mental health functioning at baseline and little change in physical health in the year prior to baseline, while subjects in the Low/Medium strata reported comparatively poorer mental health functioning and improved physical health.

**Results:** At 6-month follow-up, findings for the High propensity stratum indicated greater improvement for subjects in MTC-A overall, and for substance use and mental health in particular. In contrast, more favorable outcomes emerged for those in the C condition overall and for substance use for subjects in the Low/Medium strata.

**Conclusions:** Clients with greater psychological functioning at treatment entry and stable health may best benefit from the MTC-A program and that aftercare could help maintain, or even enhance, treatment gains achieved during residential treatment.

**Support:** This study was supported by a grant (1 UD1 SM52403-01/5, Integrated Residential/Aftercare TC for HIV/AIDS & Comorbid Disorders) from the Substance Abuse & Mental Health Services Administration's (SAMHSA's) Center for Mental Health Services (CMHS) with Health Resources & Services Administration (HRSA) HIV/AIDS Bureau, and the National Institutes of Health (NIH) [the National Institutes of Mental Health (NIMH), on Drug Abuse (NIDA), and on Alcohol Abuse & Alcoholism (NIAAA)], GFA No. SM 98.007, Cooperative Agreements for an HIV/AIDS Treatment Adherence, Health Outcomes, and Cost Study.

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**MODIFIED TC FOR PERSONS WITH CO-OCCURRING DISORDERS: META-ANALYSIS.**

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**Aims:** This research synthesis presents findings across three studies investigating the effectiveness of modified therapeutic community (MTC) treatment for clients with co-occurring disorders.

**Methods:** Clients in all studies were assigned to either MTC treatment or a control group (C) receiving standard services. Populations include Homeless clients (119 MTC1, 65 MTC2, 48 C), Offenders (92 MTC, 64 C), and Outpatient clients (107 MTC, 91 C). As part of an extensive analysis, outcome domains include mental health, substance use, crime, HIV-risk behavior, employment, and housing stability. Data were collected using standardized self-report instruments, administered by a trained interviewer at baseline (study/treatment entry) and 12 months post treatment completion or prison release.

**Results:** Moderate and significant MTC treatment effects emerged for five of the six outcome domains. MTC was associated with greater improvements in substance use, mental health, crime, employment, and housing. Significant differences were not observed for HIV-risk behavior. Findings indicated a consistency of effects across the studies and domains.

**Conclusions:** Given the need for research-based approaches, program and policy planners should consider the MTC when designing programs for co-occurring disorders.

**Support:** Study 1, a grant (1 UD3 SMT151558, Modified therapeutic community for homeless MICAs: Phase II Evaluation), from the Substance Abuse & Mental Health Services Administration (SAMSHA), Center for Mental Health Services (CMHS) / Center for Substance Abuse Treatment (CSAT), Cooperative Demonstration Program for Homeless Individuals;

Study 2, Grant 2 P50 DA07700.0003, Modified TC for MICA Inmates in Correctional Settings, National Institutes of Health (NIH), National Institute on Drug Abuse (NIDA);

Study 3, a grant (5 KD1 TI12553, Dual Assessment & Recovery Track (DART) for Co-Occurring Disorders), from SAMSHA, CCSAT, GFA TI 00-002 Grants for Evaluation of Outpatient Treatment Models for Persons with Co-Occurring Substance Abuse & Mental Health Disorders (short title Co-Occurring Disorders Study).

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**RELIABILITY AND VALIDITY OF THE SHORT INVENTORY OF PROBLEMS MODIFIED FOR DRUG USE.**

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**Aims:** The Short Inventory of Problems (SIP) assesses alcohol consequences, and has been modified to assess alcohol and drug use consequences (SIP-AD) but not drug use alone. We evaluated the reliability/validity of the SIP modified for drug use consequences (SIP-D) in detoxification unit (DU) and primary care (PC) patients.

**Methods:** Data were obtained from two sources: a randomized trial of chronic disease management (the Addiction Health Evaluation And Disease management (AHEAD) study (n=416 DU subjects), and a cross-sectional anonymous study of screening and assessment tools in a PC sample that reported past-year illicit drug use (n=104). We calculated total and subscale SIP-D scores. Cronbach's alpha assessed intrascale reliability. Spearman's rho assessed correlation with the Addiction Severity Index (ASI) drug score and number of drug dependence criteria met in the DU sample and the Drug Abuse Screening Test (DAST-10) and number of drugs detected on saliva testing (cocaine, methamphetamine, THC, opiates or benzodiazepines) in the PC sample.

**Results:** SIP-D scale reliability in both samples was high (Cronbach's  $\alpha = 0.95$  in each). The SIP-D subscales had moderate/strong reliability in the DU sample (Physical=0.78; Social=0.88; Interpersonal=0.83; Intrapersonal=0.88; Impulse Control=0.71) and PC sample (Physical=0.69; Social=0.83; Interpersonal=0.80; Intrapersonal=0.83; Impulse Control=0.73). In the DU sample moderate correlation was observed with the ASI Drug Score ( $p=0.50$ ) and number of drug dependence criteria met ( $p=0.39$ ). In the PC sample, strong correlation was seen with the DAST-10 ( $p=0.71$ ) but number of drugs detected on saliva testing had poor correlation ( $p=0.16$ ).

**Conclusions:** The SIP-D has satisfactory properties for assessing drug use consequences. Our results reinforce previous findings of the SIP instruments' ability to measure consequences in a variety of settings.

**Support:** NIAAA/NIDA grants AA010870/DA010019

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### STRUCTURAL BRAIN DIFFERENCES BETWEEN MALE ADOLESCENT PATIENTS WITH SERIOUS SUBSTANCE AND CONDUCT PROBLEMS AND CONTROLS: COMPARING TWO AUTOMATED ANALYTIC METHODS AND EXAMINING CORTICAL THICKNESS.

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**Aims:** Adolescent substance use disorders and conduct disorder are common and cause serious morbidity and mortality. Relatively few studies have tested for structural brain differences in such adolescents.

**Methods:** We recruited 25 male patients from a university-based treatment program for adolescents with serious substance and conduct problems and 19 male adolescent controls similar in age, race/ethnicity and zip code of residence (all right-handed). We have recently described patient-control differences in this sample utilizing voxel-based morphometry (VBM). Now, we re-analyze those data with FreeSurfer to test reliability across these two automated methods and to test for patient-control differences in frontal/temporal cortical thickness.

**Results:** VBM-FreeSurfer measured cortical white (WM) and gray (GM) matter were highly correlated for patients (WM  $r=0.98$ ;  $p<0.01$ ; GM  $r=0.86$ ;  $p<0.01$ ) and controls (WM  $r=0.96$ ;  $p<0.01$ ; GM  $r=0.82$ ;  $p<0.01$ ). Our largest frontal/temporal VBM finding was mapped to the left inferior-frontal junction; utilizing FreeSurfer patients demonstrated significantly less GM in the inferior frontal sulcus ( $p=0.02$ ) and the inferior frontal sulcus plus the inferior part of the precentral sulcus ( $p=0.02$ ). Examining 40 frontal/temporal FreeSurfer parcellation units, controls demonstrated significantly greater cortical thickness than patients in the right long insular gyrus ( $p=0.007$ ). VBM results showing multiple frontal/temporal regions with patient-control differences in GM volume will also be reviewed.

**Conclusions:** We demonstrate the reliability of two commonly used methods for automated brain morphometry. FreeSurfer results, like VBM, indicate that within this sample patients have less GM volume in the left inferior frontal junction; FreeSurfer results also suggest patients may have cortical thinning in the right insula.

**Support:** DA009842; the Kane Family Foundation; DA016314

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### ARE METHADONE DOSE AND "TAKE HOME" STATUS ASSOCIATED WITH HOSPITAL ADMISSION?

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**Aims:** Although receipt of take homes and higher doses are associated with improved methadone treatment program (MTP) outcomes, impact of these factors on health care utilization is not known. We studied whether take-home dosing and high doses (i.e.  $\geq 80$  mg) were associated with decreased hospital admission among patients in a MTP.

**Methods:** Among patients enrolled in one MTP from 2/06 – 3/08, we reviewed daily electronic medical records to determine receipt of take home doses and dose  $\geq 80$  mg (the two primary independent variables) and whether the subject was admitted to the hospital on the following day (the study outcome). Days hospitalized following hospital admission, days pregnant, days incarcerated, and 90 days following program admission were excluded. We used mixed effects logistic regression models to evaluate whether receipt of take homes and high doses of methadone as time-dependent variables were associated with a hospital admission on the following day. Covariates in adjusted models included age, gender, race/ethnicity, HIV status, medical illness (e.g. diabetes), mental illness (e.g. depression), and polysubstance use (e.g., cocaine use) at program admission.

**Results:** Subjects ( $n=138$ ) had the following characteristics: mean age 43 years; 52% female; 17% HIV-infected; 32% medical illness; 40% mental illness; and 52% polysubstance use. During follow-up, 42 patients (30%) accounted for 80 hospitalizations. The mean duration of follow-up was 20 months. In adjusted models, receipt of take homes was associated with significantly lower odds of a hospital admission (OR 0.23; 95%CI: 0.04-0.42) and dose  $\geq 80$  mg was not (OR 0.93; 95%CI: 0.34-1.52).

**Conclusions:** Among MTP patients, receipt of take homes, but not dose of methadone, was associated with decreased hospital admission. Take-home status may not only reflect patient success via improved addiction outcomes, but reduced healthcare utilization.

**Support:** NIDA R25 DA13582 J. H. Samet, PI.

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### NEIGHBORHOOD DISADVANTAGE AND SUBSTANCE USE AMONG ADOLESCENTS.

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**Aims:** Little is known about how neighborhoods influence substance use among adolescents. Understanding these influences may be helpful for designing neighborhood interventions. The following research question was addressed: is neighborhood disadvantage related to type and severity of substance use among adolescents?

**Methods:** Baseline data were obtained from a randomized trial to assess the effect of atomoxetine versus placebo on ADHD and substance use disorders (SUD) in adolescents receiving cognitive behavioral therapy for SUD. Data used here were from 60 adolescents (ages 13-19) living in Denver. Participants' residences were geo-coded using Geographic Information Systems software. Neighborhood data (percent of adults in poverty, percent of children in poverty, percent of adults aged 25+ with less than 12th grade education, crime rate per 1,000 residents, and violent crime rate per 1,000 residents) were obtained from the Piton Foundation. The outcome variables were self-reported number of days used alcohol, tobacco, marijuana, and non-tobacco substances in the past 28 days. In exploratory analyses, neighborhood variables were entered in forward multiple regression models that adjusted for adolescents' age.

**Results:** After controlling for age, 17% of the variability in tobacco use and 18% of the variability in alcohol use was explained by percentage of adults with less than 12th grade education in a neighborhood ( $F_{2,57}=6.89$ ,  $p=0.002$  and  $F_{2,56}=7.34$ ,  $p=0.001$ , respectively). We found less tobacco use and more alcohol use in neighborhoods with a greater percentage of adults with less than 12th grade education.

**Conclusions:** More research needs to be completed to explain the negative relationship for tobacco and the positive relationship for alcohol with neighborhood education. Knowing more about these neighborhood influences may aid in developing policy and community interventions that target neighborhood disadvantages related to substance use.

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### HOW DOES RELIGIOSITY PREVENT SUBSTANCE USE AMONG ADOLESCENTS?

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**Aims:** Assess through focus groups, religious-based preventive interventions in substance use field amongst youth from 3 religious practices.

**Methods:** Six focus groups (FG) were executed within 55 young drug-naïve belonging to different religions (18 Catholics, 19 Protestants and 18 Spiritists), the three most prevalent religious groups in Brazil. Ages ranged from 16 to 24 years. FG sessions lasted an average of 1.5 h and were recorded, transcribed and submitted to content analysis.

**Results:** Catholics and Spiritists considered the consumption of licit drugs as less harmful than illicit ones, and especially tolerated the use of alcohol. Protestants were more emphatic when describing all drugs as being harmful to one's health. They emphasized that religiosity had an important role in the decision in avoiding drugs. However, it was perceived that this 'antidrug' posture reflects much more of a family guidance than a religious belief, once they mentioned that their decision to not use drugs would happen despite of religion, based on the strength of family bonding and the need to preserve their parents from possible sufferings. None however were able to point out specific existing activities in their religious groups aiming to prevent drug use, but underscored the importance of having a network of non-users as friends. Among Protestants, a pastor preaching against drug consumption was considered as a direct form of prevention. As for Catholics, the church indirectly provides prevention as it offers substituting pleasure of experiencing holiness. The Spiritists explained the origin of drug use as combination of biological and spiritual factors, and for this reason prevent cannot be established solely on religious arguments.

**Conclusions:** In this group, the foundation that religiosity is a protective factor against drug consumption is not based just in faith, but rather the organization of a social support network formed by non-users. The interviewee emphasized the role of family supervision as a more protective agent than religion.

**Support:** FAPESP, CNPq, AFIP

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### CORTISOL SECRETION PROFILE IS ASSOCIATED WITH DROP-OUT AND MORE PERSISTENT COCAINE CRAVING DURING A TRIAL OF MIRTAZAPINE FOR THE TREATMENT OF DEPRESSED COCAINE ABUSERS.

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**Aims:** For cocaine abusers, frequent cocaine use acts as an external stressor that can disrupt the HPA axis and cortisol secretion. We hypothesized that more severe disruption of the HPA axis may indicate greater severity of cocaine dependence. To explore this, we measured cortisol secretion during an ongoing 8-week placebo controlled trial of mirtazapine for cocaine dependence and comorbid depression. Patients deemed mood responders at week 8 continued in the trial for another 8 weeks until week 16.

**Methods:** Seventy patients (58=male) meeting DSM-IV criteria for major depression or dysthymia and cocaine dependence have enrolled thus far. Salivary cortisol levels were examined at baseline, week 8 and week 16, by having patients collect saliva samples at 9am, 2pm and 5pm during a single 24-hour day. Forty patients completed saliva collection at baseline, 15 at week 8, and 7 at week 16. Cortisol secretion profiles were deemed typical (TYP) if they displayed a peak at 9 am followed by decreased levels at 2 and 5 pm. Profiles that differed from this pattern were termed atypical (ATYP).

**Results:** A Kaplan-Meier curve was used to analyze the relationship between participants' cortisol secretion profiles and weeks completed. Participants with ATYP profiles completed significantly fewer study weeks ( $M=9.63$ ,  $SD=1.33$ ) than those with TYP profiles ( $M=14.2$ ,  $SD=1.53$ ),  $\chi^2=4.696$ ,  $p=.03$ . Cocaine craving were compared between ATYP and TYP groups during the first 8-week period. Patients ATYP at baseline craved cocaine on significantly more days during the first 8 week period ( $M=45.27$ ,  $SD=15.67$ ) than those TYP at baseline ( $M=30.18$ ,  $SD=16.6$ ),  $t(20)=-2.19$ ,  $p=.04$ .

**Conclusions:** Atypical cortisol secretion profiles may indicate a greater degree of cocaine addiction severity, leading to early drop out and persistent cravings to use cocaine during treatment. Other stress parameters are being investigated as well. How to restore homeostatic stress function during treatment for cocaine dependence and depression is being scrutinized in our laboratory.

**Support:** NIDA # P50DA09236

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### GENDER DIFFERENCES IN PAST MONTH MARIJUANA USE BETWEEN INDIVIDUAL AND TEAM SPORT PARTICIPANTS AMONG 10TH GRADERS: UNITED STATES, 2006.

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**Aims:** To examine possible gender differences on how individual and team sport participation relate to past month marijuana use (MJU).

**Methods:** Monitoring the Future (MTF) survey assessed a national probability sample of 8th and 10th graders from public and private schools in the United States ( $n=16,620$ ). The 10th graders in this study consisted of 5,552 students who responded to Form 1 survey. Participants were classified in three mutually exclusive groups: No sport (NS), team-sports only (TS), and individual-sports only (IS). We estimated gender differences linking type of sport participation with past month MJU. Logistic regression was used to obtain weighted estimates. Race, mother's education, MJU peer pressure, time spent alone after school, school grades and frequency of participation in sports, athletics or exercising were included in the model to obtain adjusted odds ratio (aOR) estimates.

**Results:** Among TS participants, a higher proportion of females (26.7%) reported MJU in the past month than males (18.4%). In contrast, Males-IS participants reported a higher proportion (28.7%) of past month MJU than females (19.5%). Compared to NS, crude OR estimates were 1.4 ( $p=0.004$ ) for Females-TS and 0.5 ( $p<0.001$ ) for Males-TS. No crude association was found for both genders between MJU and IS. Adjusting for the covariates mentioned above an inverse relationship was observed for Males-TS ( $aOR=0.4$ ;  $p<0.001$ ) and a positive one for Females-TS and Females-IS ( $aOR=2.1$ ;  $p<0.001$  and  $aOR=2.1$ ;  $p=0.005$ , respectively).

**Conclusions:** Competitive sport participation, either TS or IS sports, does not seem to reduce chances of MJU during the past month for females. Assuming that any competitive sport involvement during early adolescence might lead to MJU prevention for males as well as females is not supported by these data. Further studies are needed to confirm our findings.

**Support:** None

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### D-CYCLOSERINE ATTENUATES REACTIVITY TO SMOKING CUES IN NICOTINE-DEPENDENT SMOKERS.

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**Aims:** Cue exposure treatment (CET) attempts to reduce conditioned reactions to substance cues and enhance skills training. Once seen as a promising technique for the treatment of addiction, a recent meta-analysis showed no consistent evidence for CET's efficacy (Conklin & Tiffany, 2002). Increasing evidence indicates that smoking cues contribute to nicotine self-administration and attenuating conditioned reactivity to smoking cues may aid abstinence of smoking and prevention of relapse in individuals with nicotine dependence. Pharmacological interventions that target the extinction of fear in anxiety disorders may have potential applicability to cue-exposure extinction paradigms in addiction. Based on prior studies showing that the partial N-methyl-D-aspartate agonist D-cycloserine (DCS) facilitates extinction of learned fear during behavioral exposure therapy in humans (Ressler et al. 2004; Hofmann et al. 2006) and facilitates extinction of cocaine-induced conditioned place preference in animals (Botreau et al. 2006), we evaluated whether DCS would have potential for reducing reactivity to smoking cues when combined with CET in humans with nicotine dependence.

**Methods:** In this double-blind placebo controlled pilot study, 25 nicotine dependent smokers were randomized to 2 sessions of DCS or placebo plus smoking cue exposure therapy. Participants were not required to quit smoking during the 4-week study trial.

**Results:** DCS significantly attenuated smoking cue reactivity in response to in-vivo smoking cues based on physiological reactivity and subjective urge-to-smoke ratings and led to a significantly smaller expired carbon monoxide level at 1-week follow-up compared to placebo. Exploratory analyses indicated no effect on smoking behavior overall.

**Conclusions:** These findings provide preliminary support for DCS combined with cue exposure treatment in attenuating conditioned reactivity to smoking cues.

**Support:** Funding came from NIDA grants: P50-DA009241, K05-DA00457 (Dr. Carroll), K05-DA00089 (Dr. Rounsaville), and US Dept. of VA VISN I MIRECC.

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### OUTREACH FAMILY INTERVENTION FOR YOUNG OUT-OF-TREATMENT DRUG USERS.

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**Aims:** To design, implement and evaluate an outreach family intervention for low-income out-of-treatment drug users younger than 21 years.

**Methods:** Quasi-experimental design with an experimental group (EG;  $n=65$  drug users with their families) and a control group (CG;  $n=65$  drug user). Drug users of both groups are being recruited in the community by outreach workers. Additionally to the outreach work, the EG will receive 15 to 20 sessions (in their homes) of a Brief Family Therapy. For this purpose, 10 clinical psychologists were trained in the Brief Strategic Family Therapy by the Center for Family Studies at the University of Miami. The CG will receive the usual outreach work. Outcome assessments (Addiction Severity Index 6, GHQ-12, How is your family Questionnaire, Family Environment Scale, Revised Behavioral Problem Checklist, Parenting Practices Questionnaire) will be conducted in both groups at recruitment, post intervention and 6 month follow-up. Process evaluation will be done employing the Working Alliance Inventory every four sessions.

**Results:** 18 experimental subjects and 10 control subjects have been recruited so far (ongoing study). The mean age of EG is 17 years ( $SD=1.6$ ) and of CG is 18 years ( $SD=1.4$ ). All subjects are dependent on marihuana. 13 subjects of the EG and 6 of the CG are cocaine dependent. Until now, subject in the EG have received 5 to 9 family sessions. Outcome and process information is being collected.

**Conclusions:** The EG is expected to have a higher reduction in risk behaviors, improvement in family functioning and higher entry into the national network for addiction treatment than the CG.

**Support:** Funded by FONDECYT (Grant 1085245).

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### A PRELIMINARY INVESTIGATION INTO THE ROLE OF FAMILY ENVIRONMENT, PERSONALITY, AND POSITIVE SCHIZOTYPY IN PREDICTING SUBSTANCE USE DISORDERS IN SOCIAL ANHEDONICS AND CONTROLS.

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**Aims:** Schizophrenia is characterized by high rates of comorbid substance use disorders (SUDs). Unfortunately, the factors that give rise to high substance use in schizophrenia are as yet unknown. It may be productive to examine how schizophrenia-spectrum characteristics are associated with substance use in populations that are not yet ill. The current study examined how social anhedonia (a putative indicator of risk for schizophrenia spectrum disorders) is associated with SUDs. We also examined the role of individual differences in family environment and personality traits.

**Methods:** This study utilized participants in the Maryland Longitudinal Study of Schizotypy, a study that screened 2,434 18-year-olds in the community. Two groups were selected based on initial self-report scores: individuals high in social anhedonia (N=86) and a healthy control group with low schizotypy scores (N=89). Participants completed structured diagnostic interviews at a baseline assessment and again at a 3-year follow-up. SUDs were measured dichotomously.

**Results:** Social anhedonics had significantly less education, less family cohesion, higher negative affect, and PerAb scores than controls. In social anhedonics, at baseline, family cohesion and perceptual aberration were significantly associated with having a substance use disorder ( $p's < .05$ ). Only perceptual aberration was significantly correlated with SUDs at follow-up in this group. Negative affect, disinhibition, and magical ideation were not significantly associated with SUDs in this group both at baseline and follow-up. In the control group, disinhibition was associated with SUDs at baseline and follow-up ( $p's < .05$ ). There were no other significant associations in the control group at baseline or follow-up.

**Conclusions:** These findings suggest that family environment may play a role in the development of substance use disorders in social anhedonics. Implications of other findings in this study are discussed.

**Support:** This research was supported by National Institute of Mental Health Grant MH-51240.

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### PREVALENCE OF PAIN AMONG PRESCRIPTION-OPIOD ABUSERS.

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**Aims:** While prescription opioid (PO) abuse has increased dramatically in recent years, the demographic and other characteristics of PO abusers have gone relatively unexamined. In particular, there have been limited scientific efforts to examine prevalence of pain among primary PO abusers, as well as whether pain may change as a function of treatment or be associated with an individual's response to treatment.

**Methods:** We have an ongoing double-blind randomized trial evaluating an outpatient buprenorphine taper for PO abuse. Eligible subjects must meet DSM-IV criteria for opioid dependence, identify a PO (e.g., oxycodone) as their primary drug and be using it illicitly (e.g., without a valid prescription for a medical problem). Subjects are stabilized on buprenorphine (Suboxone), after which they receive a brief buprenorphine taper. While the primary focus is on opioid abstinence, this trial provides an opportunity to examine prevalence of pain in treatment-seeking PO abusers. Pain and coping strategies were assessed via the Brief Cope, Fear of Pain, Pain Catastrophizing Scale and Intolerance to Discomfort questionnaires at study intake and Weeks 1-6, 8 and 12.

**Results:** Thus far, data from 27 subjects have been collected. Current pain was reported by 27% of subjects at intake, with no significant difference in demographic characteristics between those with and without pain. Ratings of severe pain and rumination about pain significantly decreased over the course of treatment ( $p=.04$  and  $<.01$ , respectively); no change was seen in coping strategies used by subjects (e.g., active coping, planning, self-distraction). Pain status at intake was not a significant predictor of treatment outcome in these preliminary results, though additional analyses with a larger sample size will be used to answer this more definitively for the June meeting.

**Conclusions:** Overall, this randomized trial provides a unique opportunity to investigate prevalence of pain among a clinical sample of PO-dependent outpatients. This study will contribute new information on the challenging topic of pain issues among primary opioid abusers.

**Support:** Support: NIDA T32 DA007242 and R01 DA019989

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### GENDER DIFFERENCES IN ECSTASY USE, ABUSE AND DEPENDENCE.

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**Aims:** This study examined gender differences in the DSM IV adopted Ecstasy abuse and dependence criteria in a sample of young adults.

**Methods:** Data comes from a NIDA funded multisite epidemiological study, conducted in Miami, St. Louis and Sydney between 2002 and 2004. Eligible participants (N=639; 42% Females) were assessed on the Substance Abuse Module for Club Drugs (SAM-CD), Washington University Risk Behavior Assessment for Club Drugs (RBA-CD) and the Center for Epidemiological Studies-Depression Scale (CES-D).

**Results:** Mean age of the sample was 23 years (SD=5.21). Two thirds of the sample (63%) was Caucasian, educated up to high school and had a full time job in the past 12 months. Majority was never married (93%). Significant gender differences were found only on age and employment status, with males being significantly older ( $t=3.77^{***}$ ), and greater number of males having had a full time job in the past 12 months compared to females ( $X^2=9.51^{**}$ ). Data on drug use (other than Ecstasy) indicates that the mean number of drugs used by males was significantly higher than females ( $t=4.82^{***}$ ), with no significant differences on age of onset. Females had a significantly lower age of onset ( $t=3.19^{**}$ ) of Ecstasy use compared to males. Significant gender differences were not found on total number of lifetime ecstasy use, or number of days or times ecstasy used in the past 30 days. More males obtained Ecstasy by stealing ( $X^2=4.12^*$ ), as payment for a favor ( $X^2=14.43^{***}$ ) and from dealing ( $X^2=18.87^{***}$ ), while more females got Ecstasy from a partner or spouse ( $X^2=46.06^{***}$ ). Significantly greater number of males used Ecstasy at a fraternity or sorority party ( $X^2=5.06^*$ ) and at work or school ( $X^2=5.62^*$ ). Surprisingly, there were no significant gender differences on the adopted DSM IV criteria for abuse of and dependence on Ecstasy.

**Conclusions:** These findings have implications for developing community based preventive interventions for young adults.

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### TRENDS IN ECSTASY SEIZURES AND PURITY OF SEIZED ECSTASY IN CANADA.

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**Aims:** Ecstasy remains a drug of concern among Canadians yet little is known about the quality of ecstasy seized in Canada. The Drug Analysis Service (DAS) of Health Canada analyzes suspected illicit drugs submitted by the police. The aim of this study is to assess the trends and purity of ecstasy seizures across Canada.

**Methods:** All drug seizures that were analyzed by DAS from 1988 to 2007 were included in this study. Using Stata 9.0, a 2-way table was developed on drug by province and sorted by year of seizure. Ecstasy includes all seizures of MDMA, MDA and MDEA.

**Results:** Prevalence of ecstasy seizures analyzed in Canada has increased from 0.01% (n=63) in 1989-1992 to 3.4% in 2003-2007 (n=21,059). In 2003-2007, the most commonly analyzed substances were marijuana (41.5%), cocaine (22.9%) and crack cocaine (5.2%). Over the 19 year period, the province of Ontario was found to have the highest number of ecstasy samples analyzed (n=12,456), followed by Quebec (n=8270) and British Columbia (n=4660). From 1988-2007, 67,937 samples were suspected to be MDMA by police or border services, of these 30.9% actually contained MDMA, 23.8% contained methamphetamine. The average amount of MDMA found in seized tablets has decreased from 106mg in 2000 to 48.3mg in 2007. Although the number of adulterants being used is increasing, the three most common between 2003 and 2007 were caffeine (36.2%), methamphetamine (28.5%) and procaine (9.2%) (values are not mutually exclusive).

**Conclusions:** While MDMA seizures in Canada have increased significantly over the past 19 years, the purity of ecstasy in the seized tablets is decreasing.

**Support:** Government of Canada

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### IS MODERATE SUBSTANCE USE ASSOCIATED WITH ALTERED EXECUTIVE FUNCTIONING IN A POPULATION-BASED SAMPLE OF YOUNG ADULTS?

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**Aims:** Preclinical and human studies indicate that use of ecstasy and other substances may be associated with cognitive deficits. Executive functions so far have received less attention. The study focused on possible associations between "average" use of ecstasy, cannabis or alcohol and cognitive measures of executive functions, working memory and impulsivity in a group of users recruited from a representative epidemiological sample.

**Methods:** A total of 284 young adults (mean years of age 25.8) with a history of ecstasy, cannabis and/or alcohol use and control, subsampled from a longitudinal epidemiological study, completed the assessment battery. Subjects were unaware that they had been sampled because of their reported substance use. The test battery included tests of executive functions, working memory and impulsivity among others. Analyses are based on multiple linear regression models.

**Results:** "Average" ecstasy consumption was found to be associated with increased error-proneness and lower test completion. Higher error proneness was detected in the Stroop task, the CANTAB ID/ED shift task and a spatial working memory test. Meanwhile, higher cannabis use and more extensive alcohol consumption were associated with a higher degree of impulsiveness.

**Conclusions:** Deficits in executive functioning were less pronounced when compared to memory and attention performance deficits in this group. Further studies need to investigate, how lower test results impact on further development of these young adults.

**Support:** Supported by the German Federal Ministry of Education and Research (01 EB 0440 - 0441, 01 EB 0142).

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### MICE LACKING MULTIDRUG RESISTANCE PROTEIN 1A SHOW ALTERED DOPAMINERGIC RESPONSES TO METHYLENEDIOXYMETHAMPHETAMINE IN THE STRIATUM.

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**Aims:** Multidrug resistance protein 1a (MDR1a) has been reported to potentiate methylenedioxymethamphetamine (MDMA)-induced decreases of dopamine (DA) and dopamine transport protein in mouse brain one week after MDMA administration. In the present study, we sought to test if mdr1a wild-type (mdr1a +/+) and knock-out (mdr1a -/-) mice differentially handle the acute effects of MDMA on the nigrostriatal DA system 0-24 hr following a single drug injection.

**Methods:** Striatal DA and dihydroxyphenylacetic acid (DOPAC) concentrations were measured using high-performance liquid chromatography in mice 0-24 hr following a single intra-peritoneal MDMA (10, 20 or 40 mg/kg) injection (n=5 mice per timepoint). Striatal concentrations of MDMA and its metabolite methylenedioxymethamphetamine (MDA) were measured by gas chromatography-mass spectrometry.

**Results:** 3-way ANOVA revealed significant 2-way interactions of strain X time ( $F_{3,152} = 32.4$ ,  $p < 0.001$ ) and strain X dose ( $F_{3,152} = 25.8$ ,  $p < 0.001$ ) on DOPAC/DA ratios in mdr1a +/+ and -/- mice. DOPAC/DA ratios were increased in mdr1a +/+ mice 0-3 hr after 10mg/kg MDMA, but were decreased 0-1 hr after MDMA in mdr1a -/- mice. DOPAC/DA ratios were increased 600% at 24 hr after a 10 mg/kg injection of MDMA to mdr1a +/+ mice in comparison to saline-treated control mice whereas DOPAC/DA ratios were unchanged in mdr1a -/- mice. Striatal concentrations of MDMA and MDA were similar in both strains 0.33-4 hr after MDMA.

**Conclusions:** Increased DOPAC/DA turnover in mdr1a +/+ mice following MDMA is consistent with the previous report that MDR1a potentiates MDMA neurotoxicity. Increased DA turnover via monoamine oxidase in mdr1a +/+ vs -/- mice might increase exposure of these mice to neurotoxic reactive oxygen species. MDR1a-facilitated drug distribution does not appear to play a role in these effects.

**Support:** Supported by NIDA-IRP, NIH.

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### LEISURE TIME ACTIVITIES THAT PREDICT INITIATION, PERSISTENCE, PROGRESSION, AND REDUCTION OF CANNABIS USE: A PROSPECTIVE, POPULATION-BASED PANEL SURVEY.

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**Aims:** This study aimed at identifying differences in leisure time activities that predicted different phases of cannabis use.

**Methods:** In a prospective population based survey on cannabis use a cohort of 5025 subjects aged 13 to 29 years were assessed by telephone interview and followed up 3 years later. Different leisure time activities and the persons (e.g. partner, friend, sibling) the activities were spent with were analyzed for the initiation, persistence, progression, and reduction/cessation of cannabis use over time using multinomial logistical regression models.

**Results:** The persons the leisure time was spent with at baseline led to a higher probability of initiation, persistence and reduction of cannabis use over time than the type of leisure time activity. There also was a tendency for tobacco use to increase during the persistence and progression phase and to remain high after a reduction/cessation of cannabis use.

**Conclusions:** The influence of persons the leisure time was spent with was of higher relevance to most phases of cannabis use than the type of leisure time activity.

**Support:** The Swiss Cannabis Monitoring Study was initiated by the Swiss Federal Office of Public Health (FOPH). The FOPH financed the Swiss Cannabis Monitoring Study (contract No 01.001316) and gave its approbation for the publication of the current study results.

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### IMPACT OF ADOLESCENTS' EXPOSURE TO NEGATIVE LIFE EVENTS, POVERTY AND WAR IN ISRAEL.

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**Aims:** This study examines associations between exposure to negative life events, poverty, war and terrorism and youth risk behaviors in Israel. We explored potential risk factors (e.g., gender and nationality- being an Arab or Jewish) as moderators and protective factors (e.g., social support) as mediators of these associations.

In addition to the test of the overall model we hypothesized that greater exposure to negative life events, poverty and war and terrorism will be associated with greater PTSD, substance use and perpetration of violence

**Methods:** A representative stratified sample of students, grades 10 and 11, during the academic year 2006-2007. 6132 students (3413 Jewish and 2719 Arab Israelis) responded anonymously to questionnaires designed to reveal students' risk behaviors and exposure to the events indicated above

**Results:** Among Jewish Israelis, poverty is associated with use of alcohol and violence and is related strongly to substance use. Among Arab Israelis, it is not associated with risk behaviors.

Exposure to war and terror is not associated with risk behaviors in Jewish students but is associated with risk behaviors in Arab students.

Application of Structural Equation Modeling revealed that the conceptual model is a good fit for the data. Negative life events had direct effect to use of violence and drugs. Poverty has no strong direct links with risk behaviors but the link is mediate by life satisfaction. Exposure to war and terrorism has direct links with posttraumatic stress symptoms and risk behaviors. The protective factors examined in this study did not mediate the associations between exposure to war and terrorism and risk behavior.

**Conclusions:** Drug-related epidemiological surveys should include stress factors of poverty and exposure to war, terrorism or other disasters, if applicable. Risk and protective factors should be further explored

**Support:** The Israel Anti Drug and Alcohol Authority

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### STRAIN AND HEROIN-INDUCED EFFECTS ON ENDOGENOUS OPIOID AND GABA A RECEPTOR MRNA LEVELS IN THE CAUDATE PUTAMEN OF C57BL/6J AND 129P3/J MICE.

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**Aims:** C57BL/6J (C57) and 129P3/J (129) mice differ in their behavioral response to cocaine or heroin. To investigate the effects of heroin on the endogenous opioid receptors and ligands, and on the  $\alpha 2$  subunit of the GABA A (GABAA2) receptor, we examined the expression of these mRNAs in the caudate putamen (CPu) of male C57 and 129 mice following repeated exposure to heroin in using real time PCR.

**Methods:** A total of 125 male mice, 55 C57 and 70 129, were assigned to treatment groups given different doses of heroin (0, 1.25, 2.5, 5, 10 or 20 mg/kg). Animals in the 0 mg/kg group received i.p. injections of isotonic saline on all days of the study. Animals in the other groups received injections of heroin or saline on alternate days for a total of 8 days. Mice were sacrificed, the CPu dissected and total RNA was isolated. mRNA levels of OPR-M, OPR-K, OPR-D, POMC, pDyn, pEnk and the GABAA2 receptor were measured with real time PCR. All samples were assayed in duplicate and data were normalized to GAPDH.

**Results:** Heroin had a dose-dependent effect on the levels of OPR-M, OPR-K and POMC mRNA. Heroin did not affect the levels of OPR-D, pEnk or pDyn mRNAs. There was a positive correlation between OPR-M mRNA levels and heroin-induced locomotor activity in 129 mice but not in C57 animals, even though heroin stimulated locomotion in both strains. 129 mice had lower levels of the mRNA for pDyn in the CPu than did C57 mice and they had higher levels of GABAA2 mRNA than did C57 mice. Heroin dose-dependently increased the level of mRNA for the GABAA2 in 129 mice but not in C57 counterparts.

**Conclusions:** These results suggest strain-specific regulation of pDyn and GABAA2 expression, and strain-specific modulation of heroin-induced activity by OPR-M.

**Support:** NIH-NIDA P60-DA05130; the Arcadia Charitable Trust.

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### ABUSE POTENTIAL OF TARANABANT, A CANNABINOID 1 RECEPTOR INVERSE AGONIST: A RANDOMIZED, DOUBLE-BLIND, CROSSOVER STUDY IN RECREATIONAL POLYDRUG USERS.

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**Aims:** Taranabant is a CB1R inverse agonist that was in development for treatment of obesity. The primary hypotheses were that taranabant has abuse potential (AP) no greater than placebo and phentermine has greater AP than placebo in recreational polydrug users on Drug Liking visual analogue scale (VAS) and Addiction Research Center Inventory (ARCI) Morphine Benzedrine Group (MBG). The AP of dronabinol vs. placebo, taranabant vs. phentermine and dronabinol, and motor, cognitive and safety effects were also assessed.

**Methods:** Stimulant and cannabis experienced polydrug users (N=30) were randomized in a double-blind crossover study to receive taranabant 2, 4, 10 and 20 mg, phentermine 45 and 90 mg, dronabinol 20 mg and placebo. To qualify, subjects completed a randomized crossover with d-amphetamine 15 mg and placebo. VASs, ARCI, Short-Term Memory (STM) and Divided Attention test (DAT) were administered over 24 hours and peak or change from baseline effects were analyzed using a linear mixed effects model.

**Results:** Phentermine 45 and 90 mg showed greater AP than placebo on Drug Liking (LS mean differences=18.17 and 28.31,  $p<0.001$ ), MBG (5.24 and 6.58,  $p<0.001$ ) and other measures. Taranabant 20 mg had no greater AP than placebo on Drug Liking (-3.86 with 95% CI [-10.72, 3.00]), MBG (1.06 with 95% CI [-0.64, 2.77]) or most other measures. Comparisons of lower doses of taranabant to placebo showed similar results. Dronabinol had AP greater than placebo (Drug Liking: 14.92,  $p<0.001$ ; MBG: 3.31,  $p<0.001$ ) and impaired motor/cognitive performance. Taranabant 4 and 20 mg had minor effects on manual tracking, but no other impairment effects. Taranabant was significantly different from phentermine and dronabinol on most measures.

**Conclusions:** These results confirm that phentermine and dronabinol have significant AP. In contrast, the CB1R inverse agonist taranabant did not show AP or stimulant/cannabis-like effects.

**Support:** This study was sponsored by Merck & Co Inc.

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### ROLE OF INHIBITORY NEUROSTEROIDS IN REDUCING COCAINE SELF-ADMINISTRATION AND CUE-INDUCED REINSTATEMENT.

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**Aims:** Several compounds which potentiate GABA-induced inhibitory currents can also decrease stress, anxiety and addiction-related behaviors. Because of the well-established connection between stress and addiction, compounds which reduce stress-induced responses could be efficacious in treating addiction. Endogenous neurosteroids such as allopregnanolone may function similarly to benzodiazepines to reduce HPA axis activation and anxiety following stressful stimuli. We hypothesized that exogenously applied neurosteroids would be able to reduce cocaine seeking in two animal models.

**Methods:** Male Wistar rats (n=12) were trained to self-administer cocaine and food under concurrent alternating FR4 schedule. A separate group of rats (n=14) was trained to self-administer cocaine and exposed to cue-induced reinstatement following forced abstinence. Both groups were administered vehicle or several doses of neurosteroid in random dose order 30 minutes (IP route) or 15 minutes (ICV route) prior to the self-administration or reinstatement session.

**Results:** Allopregnanolone and R6305-7 were ineffective in selectively decreasing cocaine self-administration. Both neurosteroids decreased food self-administration, suggesting a general decrease in motivation or locomotor activity. Both allopregnanolone and R6305-7 by IP injection were able to decrease reinstatement responding, confirmed by one-way ANOVA.

**Conclusions:** In conclusion, these data do not support selective effects of neurosteroids in reducing drug-taking behavior during the maintenance phase of cocaine addiction. Interestingly, these results suggest that neurosteroids may be effective in reducing relapse to cocaine-seeking behavior mediated by drug-associated environmental stimuli.

**Support:** Supported by DA06013

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### EFFECTS OF MOTIVATIONAL INTERVIEWING AND COGNITIVE BEHAVIORAL THERAPY ON PEOPLE WITH CO-OCCURRING DISORDERS.

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**Aims:** A community-based effectiveness study was conducted to determine the clinical impact of a combined brief Motivational Interviewing (MI) and Cognitive Behavioral Therapy (CBT) protocol for persons with co-occurring mental health and substance use disorders. We hypothesized that this specific combined therapy would yield better outcomes than Treatment as Usual (TAU). We also sought to determine if MI-only, CBT-only, or MI+CBT achieved better outcomes for different clients, based on problem severity.

**Methods:** 16 therapists at 2 community mental health agencies were assigned randomly to 1 of 4 treatment conditions (MI, CBT, MI+CBT, TAU). Each group received manual guided training and clinical supervision. MI was employed for 1 or 2 individual session(s) followed by 4 sessions of CBT in the combined condition or 4 sessions of TAU for the MI-only group. A single 'placebo' session was provided (in lieu of MI) before the CBT-only and TAU conditions. 35 adult clients who were assigned randomly to treatment condition fulfilled all study requirements. All of these participating clients completed an assessment battery at baseline and exit that included the Brief Symptom Inventory (BSI) of psychiatric symptoms. Here we report on changes in participants' symptom severity—BSI global (GSI) and subscale scores—after the interventions compared to TAU and each other. Generalized Estimating Equations were used in the analysis to control for the lack of independence caused by clustering of participants under clinicians. Baseline severity (BaS), treatment condition (TC) and the BaS x TC interaction were included as predictors for each subscale.

**Results:** Treatment outcome varied as a function of BaS and TC. Thus, GSI scores improved significantly for people with moderate and high BaS in the MI+CBT group and those with high BaS in MI-only, compared to TAU. Such BaS-dependent treatment effects were found for 7 of the BSI subscales.

**Conclusions:** Practically applied, these findings indicate that clinicians should take into account the level of baseline severity, client problem and outcome of interest in selecting a treatment modality.

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### THE EFFECT OF TREATMENT SETTING ON OUTCOME IN TREATING OPIOID DEPENDENCE WITH BUPRENORPHINE.

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**Aims:** To determine if outcome after treatment with buprenorphine is associated with treatment setting and related psychosocial intervention.

**Methods:** A total of 96 participants presented for treatment and were randomized to 1 of 3 treatment settings: a group based cognitive-behavioral therapy setting (MMM, n = 34), medical management in a private physician's office (PPO, n = 33), and a research clinic resembling a typical opioid treatment program (OTR, n = 29). Each setting provided treatment with sublingual buprenorphine for up to 52 weeks (a maximum of 24mg daily), but differed in the provision of psychosocial interventions in areas such as type of counseling provided, number of weekly sessions weekly, and appointment availability. Assessments occurred at screening, twice in the first week, weekly through week 9, and monthly from weeks 10 -52.

**Results:** Recent analyses of the urine test results collected over the study duration indicate that those in the MMM group had more opiate-negative results compared to the other sites ( $p < 0.05$ ).

**Conclusions:** A discussion of these findings and results from secondary outcome measures emphasizes the need to identify optimal treatment practices for increasing positive outcome.

**Support:** NIDA grant #DA 09260

### PRELIMINARY OUTCOMES OF A BEHAVIORAL TREATMENT TRIAL AMONG OPIATE IDU IN CENTRAL UKRAINE.

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**Aims:** The aim of this randomized trial is to test the efficacy of a transported behavioral intervention for opiate injection drug users (IDU) in Central Ukraine on drug abstinence and functioning.

**Methods:** This is a preliminary analysis for 116 IDU entering addiction treatment in Vinnitsya, Ukraine with 13 months of follow-up. The experimental intervention is behavioral day treatment + standard inpatient medical care at the Regional Narcological Dispensary, plus 3 months aftercare with therapeutic goal management + vouchers. Assessments were urine test, Addiction Severity Index (ASI), Beck Depression Inventory (BDI), and Brief Symptom Inventory (BSI).

**Results:** At 1-month, 82.7% of urine tests in the experimental group were negative v. 46.9% for controls ( $p=0.0002$ , OR = 0.19 [95% CI = 0.07 – 0.46]). At 4 months, negative urine frequency was 71.7% experimental v. 42.9% controls ( $p=0.0088$ , OR=0.3 [95% CI=0.12-0.75]). The 7- and 14-month rates did not differ. The drug ASI composite decrease was greater for experimental v. control at 7 and 13 months (-0.15 points vs -0.08,  $p=0.02$  at 2nd; -0.17 vs 0.07,  $p=0.001$  at 3rd). The experimental group showed improved psychiatric status at both points, but controls worsened (-0.06 vs +0.02,  $p=0.08$ ; -0.16 vs +0.01,  $p=0.001$ ). Baseline ASI family/social functioning was worse in experimental v. control (0.62 vs 0.47,  $p=0.008$ ) while the experimental group showed greater improvement at 13 months (-0.23 vs -0.07,  $p=0.04$ ). Psychological distress (BSI) decreased more in experimental v. control group at 7 and 13 months (-0.67 vs. -0.23,  $p=0.002$ ; -0.76 vs -0.30,  $p=0.002$ ). Follow-up rates were 70% to 91% across all points and treatment groups.

**Conclusions:** The transported behavioral treatment appears to be successful upon treatment completion especially for the experimental condition.

**Support:** This project is funded by NIDA grant # 5R01DA18240.

### HEAD INJURY AND INTIMATE PARTNER VIOLENCE PERPETRATION AMONG ALCOHOL-TREATMENT SEEKING MEN.

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**Aims:** Head injury has been associated with both physical intimate partner violence (IPV) and alcohol dependence (AD) (Rosenbaum & Hoge 1989; Koponen et al., 2002). Additional research suggests men who engage in IPV exhibit deficits in executive function and impulse control (Cohen et al., 1999, 2003). Although cognitive deficits and elevated rates of IPV have been found in AD treatment samples (Bates et al., 2002; O'Farrell & Murphy, 1995), head injury and cognitive deficits have not been well studied as predictors of IPV in these samples. Consistent with research comparing men in batterer treatment to non-violent controls, we hypothesized that AD treatment seeking men who reported IPV would be more likely to report history of head injury and exhibit impaired executive function and heightened impulsivity relative to non-violent men.

**Methods:** To date, 59 male AD treatment seekers who were involved in a serious heterosexual relationship have provided complete data in this ongoing study. Forty-eight met criteria for at least one other substance disorder, and 34 reported past year IPV perpetration. Participants completed self-report, neuropsychological, and laboratory measures of relevant constructs.

**Results:** Preliminary results are somewhat consistent with hypotheses: men reporting head injury were more likely to report injuring a partner ( $\chi^2 = 6.0$ ,  $p = .01$ ) and there was a trend toward greater reports of IPV ( $\chi^2 = 3.3$ ,  $p = .07$ ). Men who reported IPV indicated greater impulsivity on the Barratt Impulsiveness Scale,  $t(1, 57) = 2.2$ ,  $p = .03$  and the Eysenck Impulsivity Scale,  $t(1, 57) = 2.2$ ,  $p = .03$ , and showed a trend toward significantly poorer function on Digit Symbol,  $t(1, 53) = 1.69$ ,  $p = .10$ , but did not differ on the Go-Stop task or Category Test.

**Conclusions:** Preliminary findings from this study suggest cognitive and behavioral factors which differentiate batterers from controls may help us understand why some, but not all men in AD treatment are at heightened risk for IPV perpetration.

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### INTERIM VS. COMPREHENSIVE VS. RESTORED METHADONE TREATMENT: PRELIMINARY FINDINGS.

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**Aims:** Interim methadone (IM) consists of methadone without counseling for individuals on waiting lists for methadone treatment programs (MTP). The present study is comparing the effectiveness and cost-benefit of IM treatment with two other levels of counseling provided with methadone to newly enrolled patients in two MTPs in Baltimore.

**Methods:** 300 opioid dependent adults on waiting lists for two MTPs are being randomly assigned to: IM (with emergency counseling only), comprehensive methadone (CM – with counseling as usual) and restored methadone (RM – with a counselor with a reduced caseload). In RM, the counselor has a caseload that more resembles the typical caseload at the inception of methadone treatment so that she can provide a more individualized level of counseling and case management. The Addiction Severity Index is being administered at baseline and 2, 4, and 12 months post-baseline.

**Results:** To date, 80 participants have been enrolled with a mean age of 43.1 years old (SD=8.4). Participants are 70% male, 73% African American, and 26% White. There were no significant differences among the conditions at baseline in terms of the number of self-reported days of heroin or cocaine use, or of the amount of money obtained from illegal sources (all  $ps > .19$ ). At 2-month post-baseline (n = 33) the mean (SD) number of self-reported days of heroin use in the last 30 days for the IM, CM, and RM Conditions were, respectively: 1.5 (1.8), 2.4 (4.5) and 3.9 (8.0), while the number of days of cocaine use were 1.1 (2.4), 0.3 (0.8), and 0.9 (1.4).

**Conclusions:** This ongoing trial will provide data on drug use, criminal behavior and cost-benefit to inform the role IM can play when access to standard treatment is limited.

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### COMMUNITY REINFORCEMENT APPROACH FOR COCAINE DEPENDENCE IN A COMMUNITY SETTING: INDIVIDUAL- VS. GROUP-BASED INTERVENTION.

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**Aims:** There is extensive clinical evidence that some behavioural and psychosocial treatments are effective in the treatment of cocaine addiction. The main objective of the present study was to analyze the effectiveness and the applicability of the Community Reinforcement Approach (CRA) in a Spanish public healthcare context. A second objective was to determine the differential efficacy of the CRA applied individually- vs group-based.

**Methods:** Forty-one cocaine dependent patients enrolled on an outpatient program for cocaine dependence were assigned to one of two treatment conditions, CRA in individual format (CRA-i) or CRA in group format (CRA-g). The CRA therapy comprises five components: Drug avoidance skills, lifestyle change components, relationship counseling, other substance abuse and other psychiatric problems. The CRA was manual guided (Budney and Higgins, 1998).

**Results:** Outcomes after 6 months of treatment indicated the same retention (60%) in both groups. Twenty six point nine percent of the patients in the CRA-i achieved 24 weeks of continuous cocaine abstinence, versus 40.7% in the CRA-g. Of the patients who received CRA-i, mean duration of continuous cocaine abstinence was 10.5 weeks versus 13 weeks of the patients who received CRA-g.

**Conclusions:** These initial results suggest that CRA can be an effective intervention approach in a public healthcare context in Spain. It does not seem that the group format adversely affects the effectiveness of the CRA plus vouchers program. Even so, the retention and consumption rates are slightly better in the CRA-g than in the CRA-i. Therefore, group-based intervention should be considered as an alternative way of reducing the costs of the CRA program in community settings.

**Support:** Supported by Spanish National Plan on Drugs (Ref. MSC-06-01) and the University of Oviedo, Spain.

### SIGMA ANTAGONISTS, AC927 AND CM156, PROTECT AGAINST METHAMPHETAMINE-INDUCED SEROTONIN DEPLETION WHILE ATTENUATING HYPERTHERMIA.

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**Aims:** Methamphetamine (METH) acts as central nervous psychostimulant damaging both dopaminergic and serotonergic nerve terminals within the brain. While the majority of METH research is designed around mitigating the dopamine effects, serotonergic damage is thought to play a significant role in METH-induced complications. 5-HT and sigma receptors have been found to mediate the role of METH in the brain. In the present study two sigma antagonists, AC927 and CM156, were evaluated for their ability to protect against serotonin depletion following METH treatment as well as attenuating METH-induced hyperthermia.

**Methods:** Male Swiss Webster mice were assigned to one of 4 experimental groups: (1) Saline + Saline; (2) Saline + METH (0-10 mg/kg); (3) AC927/CM156 (0-20 mg/kg) + Saline; (4) AC927/CM156 (0-20 mg/kg) + METH (0-10 mg/kg). The mice received four injections of their designated treatment at 2 h intervals. Body Temperature was taken 1 hour following each of the four injections and an ELISA was run to measure serotonin levels in the striatum.

**Results:** Serotonin was significantly reduced in the striatum ( $P < .0001$ ) following METH treatment. Pretreatment with AC927 significantly attenuated the ability of METH to produce neurotoxic effects in the striatum ( $p < .001$ ). Similarly, pretreatment with CM156 also significantly attenuated METH-induced neurotoxicity in the striatum ( $p < .001$ ). Additionally, METH was shown to increase body temperature in a dose dependent manner. However, pretreatment with either sigma antagonist AC927 or CM156 significantly attenuated the ability of METH to produce its hyperthermic effects ( $p < .0001$  and  $p < .001$ , respectively).

**Conclusions:** Both sigma antagonists AC927 and CM156 demonstrate a significant protection against serotonin depletion and METH-induced hyperthermia. These compounds may represent a viable treatment for complications resulting from METH abuse.

**Support:** This work was supported by the National Institute on Drug Abuse (DA023205, DA013978)

### LACK OF ABUSE POTENTIAL OF TESOFENSINE IN RECREATIONAL STIMULANT USERS.

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**Aims:** Tesofensine (TESO) is a noradrenaline, dopamine and serotonin reuptake inhibitor in development for the treatment of obesity. A delayed onset (7 hrs) and long half-life (200 hrs) suggest that TESO should have low abuse potential. The aim of the study was to evaluate the abuse potential of TESO vs placebo (PBO), d-amphetamine (AMP), bupropion (BUP) and atomoxetine (ATO).

**Methods:** A single dose, randomized, double-blind, nested crossover with 3 TESO doses (1, 6 and 9 mg) vs PBO, 15 and 30 mg AMP, 400 mg BUP and 100 mg ATO in recreational stimulant users (N=52). Due to TESO's long half-life, PBO and comparators were given fully crossed over, while in the last 2 periods, 3 parallel groups (N=13-16 each) received 1 TESO dose in a 2x2 crossover with PBO. Visual analogue scales (VASs), Addiction Research Center Inventory (ARCI) and other measures were administered over 48 hrs and peak effects were analyzed by linear mixed model and t-test.

**Results:** AMP had significantly greater effects vs PBO on all primary variables: Drug Liking, Overall Drug Liking, ARCI MBG and ARCI Amphetamine, and all 4 secondary positive/stimulant measures ( $p \leq 0.008$ ). TESO was not different from PBO on any primary variables. Any Effects VAS was not statistically different from PBO indicating that TESO effects were not readily detected. TESO had significantly lower effects than AMP on most measures and lower effects than BUP and ATO on some measures (Drug Liking, Any Effects (vs. BUP), Any/Good Effects, High, ARCI PCAG (vs. ATO), particularly at 9 mg).

**Conclusions:** Significant positive, euphoric, stimulant and other effects of AMP confirmed study validity. TESO did not have significant positive, euphoric, stimulant or other effects at doses ranging from 1 mg (maximum therapeutic dose) to 9 mg. The TESO dose-effect relationship was flat or negative and its effects were consistently lower than AMP (and BUP/ATO in some cases). The results indicate that TESO has no or very little abuse potential.

**Support:** This study was sponsored by NeuroSearch A/S.

### USING A COMMUNITY COALITION TO DEVELOP A SMOKING CESSATION PROGRAM TO REDUCE INFANT MORTALITY.

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**Aims:** In Richmond, VA, rates of infant mortality (IM) are 4-5 times higher among African-Americans (AA) than among Caucasians. Many risk factors have been identified, but efforts to address them and reduce the disparity have been unsuccessful. The present study used CPBR methods to identify a target risk factor and develop a social marketing campaign.

**Methods:** A research/service provider coalition collected multi-method multi-source (MMMS) data. Stage 1 formative research included: 1) researcher and community partner rankings of 7 potential campaign foci, 2) IM risk factor literature review, 3) vital records analysis and survey in a local OB clinic. Stage 2 involved: 1) identifying relevant evidence-based interventions, 2) interviewing 9 national experts, 3) conducting 5 theory-based focus groups with target audience members.

**Results:** Stage 1 Survey data found smoking cessation the most important feasible maternal behavior change ranked by researchers and community agencies. Analyses of local records confirmed correlation between smoking and IM found in research literature. Local clinic survey found 39% of pregnant AA women smoked in the past 3 months. These data supported a decision to focus on tobacco use. Stage 2 Evidence-based anti-smoking programs were identified. Focus group participants reported needing cessation help but not knowing where to get it. A secret shopper found the VA Quitline was the most accessible local service. Planning is underway to encourage pregnant AA women who smoke to call the VA Quitline. The presentation will offer data from the above components and how they synergistically led to current campaign.

**Conclusions:** Agreement across MMMS findings convinced coalition members their planning decisions were on firm footing. Use of CBPR methods deepened the collaboration between "bench" researchers and "trench" community agencies. IM coalitions that follow these steps may be likely to undertake anti-tobacco initiatives.

**Support:** NIH National Center for Minority Health and Health Disparities

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**EFFECTS OF CROSS-DRUG PREEXPOSURE ON COCAINE- AND DESIPRAMINE-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 desipramine (DMI), a selective norepinephrine (NE) transporter inhibitor, and cocaine (a nonselective monoamine transport inhibitor) induce aversions by a common mechanism, specifically increases in NE activity.

**Methods:** Male Sprague-Dawley rats were exposed to DMI (Experiment 1) or cocaine (Experiment 2) prior to aversion conditioning with cocaine, DMI or vehicle. DMI and cocaine were administered subcutaneously at 18 mg/kg during both preexposure and conditioning phases.

**Results:** A 2 x 3 x 5 mixed-model ANOVA revealed significant effects of Trial, Preexposure drug and Conditioning drug in Experiment 1. Fisher LSD post hoc analysis revealed that preexposure to DMI attenuated aversions induced by cocaine in Experiment 1. The mixed model ANOVA for Experiment 2 also revealed significant effects of Trial and Conditioning drug (but not Preexposure drug). Fisher LSD post hoc analysis revealed that preexposure to cocaine did not attenuate DMI-induced aversions in Experiment 2 and, in fact, potentiated aversions induced by DMI on several trials (all  $F$ 's  $\geq 2.127$ ; all  $p$ 's  $\leq 0.036$ ).

**Conclusions:** The attenuation of cocaine-induced aversions by preexposure to DMI suggests a common mechanism underlying aversions induced by the two compounds, i.e., NE activity. The fact that cocaine preexposure potentiated DMI-induced aversions suggests that compensatory adaptations following cocaine may result in heightened NE levels in DMI-treated subjects. These results may provide insight into the mechanism underlying cocaine-induced aversions and have clinical implications for the serial use of these compounds (in individuals comorbid with depression and drug abuse).

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**PATTERNS OF COGNITIVE IMPAIRMENTS AMONG HEROIN AND COCAINE USERS AND THE ASSOCIATION WITH PREEXISTING DEVELOPMENTAL CONDITIONS AND HEPATITIS STATUS.**

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**Aims:** The current study sought to evaluate the association between patterns of performance on neuropsychological measures and preexisting conditions and if these patterns are associated with hepatitis B and hepatitis C status.

**Methods:** This study used data from the International Neurobehavioral HIV Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of infectious disease. The sample for this analysis was limited to 378 HIV negative participants reporting use of heroin, crack-cocaine and/or cocaine within the past week. Five neuropsychological measures were included.

**Results:** A latent profile analysis indicated the presence of 3 classes: an intact, low average, and impaired class. Individuals that reported being diagnosed with a learning disability in childhood were more likely to be in the impaired class ( $OR=4.10$ ; 95% CI: 3.16-28.50) than in the low average class after adjusting for years of drug use and other demographic factors. Furthermore, most likely class membership was associated with Hepatitis B and/or Hepatitis C infection; specifically, those in the intact class were less likely to be infected with Hepatitis B and/or Hepatitis C than in the impaired class ( $OR=0.46$ , 95% CI: 0.23-0.92).

**Conclusions:** The findings contribute to a growing base of literature that identifies associations between neuropsychological performance and risk factors for infectious disease among injection and non-injection drug users. These initial findings suggest that pre-existing disorders are associated with impairment on neuropsychological measures among drug users and that these impairments may be associated with disease status.

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**THE INTERACTION BETWEEN OPIOIDS AND ALCOHOL: RESULTS FROM A GLOBAL LITERATURE REVIEW.**

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**Aims:** Although the pharmacokinetic (PK) relationship between alcohol and opioids has been studied in some detail, the pharmacodynamics (PD) of alcohol-opioid interactions have not been well characterized. A global literature review was conducted to gather published data on the safety risks associated with alcohol-opioid interactions and alcohol-induced dose-dumping, and on the methodology used to characterize such interactions.

**Methods:** The literature search included randomized, nonrandomized, human, animal and in vitro studies. PubMed and EMBASE databases were used; electronically available conference abstracts were searched. There was no restriction on publication language.

**Results:** A total of 13,381 publications were identified. Sixteen clinical studies were considered most relevant. Of these, 9 studies examined the PD and safety effects of alcohol-opioid interactions; none demonstrated significant PD or safety effects found at the conditions and doses studied. Seven other studies examined dose-dumping and/or alcohol-opioid PK effects. These trials primarily assessed PK in healthy volunteers, often with a naltrexone cover, precluding any conclusions regarding PD effects. To date, opioid PK and PD studies report high degrees of inter- and intra-individual variability. Studies show the PD interaction and safety profile between alcohol and opioids differs from that between alcohol and benzodiazepines.

**Conclusions:** Limited preclinical and clinical data preclude any concrete conclusions regarding the interaction and safety risks associated with alcohol and opioid coadministration. Further studies in populations of individuals who are occasional compared with heavy drinkers and/or drug takers are required to assess the clinical relevance and safety risks associated with opioids and alcohol use.

**Support:** King Pharmaceuticals®, Inc.

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**THE IMPACT OF A CURRICULUM INFUSION ON COLLEGE STUDENTS' KNOWLEDGE AND ATTITUDES TOWARD PROBLEM GAMBLING.**

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**Aims:** To examine the impact of a brief problem gambling curriculum infusion package on students' knowledge and attitudes about gambling behavior.

**Methods:** The CIP-PG was infused into an introductory criminal justice course at the University of Nevada, Reno. Pre/post-test measures were developed based on curriculum objectives to assess students' knowledge and attitudes regarding gambling behaviors, and included 21 items that used a combination of multiple choice and 5-point Likert scale response options.

**Results:** A total of 44 students completed pre/post-test survey instruments. Using repeated-measures ANOVAs, significant positive changes in knowledge and attitudes were found. In addition, participants were presented with three scenarios and asked to rate the level of gambling difficulties indicated in each. Using a rating scale where 1 represented social/recreational gambling, 5 represented problem gambling, and 9 represented pathological gambling, mean ratings for each scenario were as follows: college students playing poker on a Friday night instead of studying received, 3.41; a woman using her food money to play slots in the grocery store, 4.89; and a father sneaking \$100 from his children's piggy-bank to buy raffle tickets from neighbor kids, 5.17.

**Conclusions:** The overall findings from this study suggest that a brief curriculum infusion is effective in changing knowledge and attitudes related to problem gambling behaviors among undergraduate criminal justice pre-service students. Such findings support the continued development and revision of this 75-minute curriculum for dissemination into other pre-service health care and social service coursework.

**Support:** Funded by the Nevada Council on Problem Gambling

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### CHARACTERISTICS OF ADOLESCENT MARIJUANA SMOKERS: ENDORSING THE NEED, AND WILLING TO PARTICIPATE IN A MJ QUIT PROGRAM.

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**Aims:** In a phone survey aimed at recruiting adolescents for a tobacco cessation trial, interviewees were asked about their marijuana (MJ) use and their opinions if a MJ quit program is needed and if they would be willing to participate in such a program.

**Methods:** The sample consisted of 575 adolescents who completed the phone survey (controls included).

**Results:** They were aged  $15.8 \pm 1.47$  years, were 43.1% female, 47.3% Caucasian and 3.1% Hispanic or Latino. Less than half (46.8%) smoked tobacco, approximately one-third (33.4%) smoked MJ, 41% used alcohol, and 7% used drugs other than tobacco, MJ or alcohol. The majority of respondents (81.2%) endorsed a need for a MJ quit program for teens. These individuals were younger and less likely to smoke tobacco (42.8% vs. 63.9%), smoke MJ (30.4% vs. 46.3%), and use alcohol (38.8% vs. 50.9%) than their counterparts who thought a MJ quit program for teens was unnecessary. MJ smokers who endorsed a need for a MJ quit program took their first puff of MJ at a slightly younger age than MJ smokers who thought a MJ quit program unnecessary ( $13.1 \pm 1.82$  vs.  $13.9 \pm 1.49$  years). MJ smokers were different from respondents who did not smoke MJ. They were older ( $16.4 \pm 1.23$  vs.  $15.5 \pm 1.49$  years,  $p < 0.0001$ ), more likely to smoke tobacco (78.7% vs. 30.8%,  $p < 0.0001$ ) and more likely to use alcohol (74.5% vs. 24.3%,  $p < 0.0001$ ) as well as other drugs (20.3% vs. 0.26%,  $p < 0.0001$ ), and more likely to report psychological problems (23.7% vs. 16.1%,  $p = 0.038$ ) compared to their counterparts who did not smoke MJ. Of MJ smokers, only race and age the respondent took his/her first puff of MJ were significantly associated with willingness to participate in a MJ quit program. Respondents who indicated willingness to participate were more likely African American (55.7% vs. 36.4%) and took their first puff of MJ at a younger age ( $13.1 \pm 1.82$  vs.  $13.9 \pm 1.49$  years).

**Conclusions:** This data suggests the development of pilot MJ quit programs would be utilized by adolescents and should be considered by healthcare providers.

**Support:** DHHS, NIH, NIDA-IRP Baltimore MD

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### SELF-ADMINISTERED COCAINE DOES NOT RESULT IN LOCOMOTOR SENSITIZATION IN MONKEYS.

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**Aims:** Behavioral sensitization (i.e., a progressive increase in behavior as a consequence of repeated drug exposure) is considered to be a model of neural adaptations to addiction circuitry in the brain following long-term drug exposure. Research conducted with humans, however, has not consistently reported behavioral sensitization following repeated cocaine treatment. To explore further the extent to which sensitization develops to the locomotor-activating effects of cocaine in monkeys, we examined changes in locomotor activity induced by repeated intravenous (i.v.) cocaine self-administration.

**Methods:** Rhesus monkeys were implanted with i.v. catheters and allowed to self-administer cocaine (0.03 mg/kg/injection) for 1 hour/day or a daily maximum of 3.0 mg/kg (100 injections) under a continuous reinforcement schedule. An additional group (yoked control) received a passive infusion of saline coinciding with each cocaine injection. Duration of cocaine exposure varied from 9 sessions (cumulative dose of approximately 30 mg/kg) to 113 days (cumulative dose of approximately 300 mg/kg). Locomotor activity was measured in 1 minute intervals, 24 hours per day using the Minimitter Actiwatch system.

**Results:** All monkeys acquired self-administration, although day-to-day self-administration varied from 20 to 100 injections per session. Compared with yoked controls, the cocaine animals exhibited no consistent increases in locomotor activity across daily self-administration sessions.

**Conclusions:** These findings suggest that under the experimental parameters of this study, behavioral sensitization does not develop following repeated cocaine exposure. Moreover, ongoing studies have shown a trend towards the development of tolerance to the locomotor effects of cocaine after greater than 30 sessions of exposure.

**Support:** DA21420, DA11792, AA16179, RR00168

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### ASSESSING ADDICTION TREATMENT INFORMATION SYSTEMS IN MARYLAND: GAPS AND REDUNDANCIES.

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**Aims:** The purpose of this study is to explore the origins of the Maryland State's active addiction treatment information systems, as well as their gaps and redundancies. This assessment examines existing data collection efforts, discusses the rationale, and recommends new interventions to improve treatment outcomes by using information systems at the local level.

**Methods:** 507 accredited treatment centers in Maryland were assessed for their types of services and their required data entry responsibilities. Three active information systems such as The University of Maryland's Automated Tracking System (HATS), State of Maryland Automated Record Tracking (SMART), and Centralized Intake and Referral Management Information System (CIRMIS) were compared based on their content, format, accessibility, and data utilization. Basic characteristics of the information systems were explored through both systematic reviews of the literature and key informants' interviews. Gaps and redundancy analysis was performed to document the areas that were covered by more than one information system or not covered at all.

**Results:** Current active information systems have major gaps and redundancies. They all collect similar information in areas such as history of drug use, type of treatment, etc. Some advanced features, such as electronic case management, treatment plan generator, and referral forms have resulted in more comprehensive data systems and reports. However, it is not clear how the information systems contributed to improve the quality of treatment services at the local level.

**Conclusions:** Addiction treatment information systems have the potential to improve the quality of clinical services and treatment outcomes. Areas such as personalized case management and tracking systems can be used by treatment centers, individually or through collaboration with other local partners, to improve treatment outcomes. These issues are not fully addressed by the information systems yet.

**Support:** National Institute on Drug Abuse, grants DA012390, DA019805; National Center on Minority Health and Health Disparities, grants MD000217 and MD002803.

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### ESTROGEN'S ANTIHYPERALGESIC EFFECTS IN PAW TISSUE OF OVARECTOMIZED RATS DURING CARRAGEENAN-INDUCED INFLAMMATION.

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**Aims:** Epidemiological studies demonstrate that estrogen attenuates the behavioral response to inflammation-induced pain. However, the mechanisms underlying estrogen's antihyperalgesic effects are not known. One way in which estrogen may be lowering pain responses is by reducing the development of inflammation. The present study assessed the effects of estrogen on inflammation in carrageenan-treated rats.

**Methods:** To this end, eight-week old ovariectomized (OVX) Sprague-Dawley female rats ( $N = 82$ ) were subcutaneously implanted with a Silastic capsule containing either 20% 17 $\beta$ -estradiol or vehicle (cholesterol). One week after implantation, right hind paw sizes (in mm<sup>2</sup>) of naïve rats were compared to paw sizes of rats injected with saline or 1% carrageenan (100 $\mu$ L injection into the intraplantar region of the right hind paw) measured at 1, 5, or 24 hours post injection.

**Results:** In all experimental groups, carrageenan significantly increased ipsilateral paw size compared to naïve and saline treatments ( $p < 0.01$ ). Further, in the ipsilateral paw, an interaction between estrogen treatment and time of injection was observed [ $F(2, 51) = 3.31$ ,  $p < 0.05$ ]; at 24 hours, OVX rats administered estrogen had significantly smaller paw sizes than other treatment groups ( $p < 0.01$ ). In the contralateral paw, a main effect for estrogen was observed [ $F(1, 56) = 8.55$ ,  $p < 0.01$ ]; estrogen treatment significantly lowered paw size in saline and carrageenan groups at all time points compared to vehicle-treated controls ( $p < 0.01$ ).

**Conclusions:** Taken together, our results show that estrogen reduces inflammation in peripheral tissue, which may be a mechanism through which estrogen decreases behavioral responses to pain.

**Support:** SCORE 506-GM00654, NIH/NIDA R24-012136, RCMI RR03037, MBRS GM06665-09, CUNY NSF/AGEP-SBE 0549066, and SNRP NS41073.

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**THE ROLE OF GABAA RECEPTORS IN SEX DIFFERENCES IN COCAINE-STIMULATED LOCOMOTION.**

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**Aims:** Recently GABA and Glutamate have been implicated in modulating behavior associated with cocaine exposure. There is little data on the roles of specific GABAA receptor subtypes in the modulation of behavioral responses to cocaine administration and on sex differences in response to GABAergic stimulation. In our experiments, we used gaboxadol (GBX), a GABAA agonist selective for the  $\alpha 4\beta 2\delta$  receptor subtype, and diazepam (DZ), a non-selective positive allosteric modulator of GABA, to determine the relative activity of the receptor subunits in dampening the cocaine-stimulated locomotor (CSL) response in male and female rats. Since females sensitize less to cocaine administration after isoflurane exposure (Dow-Edwards 2008) and  $\alpha 4\beta 2\delta$  GABAA receptors are most sensitive to isoflurane (Jia et al 2008), we hypothesized that the  $\alpha 4\beta 2\delta$  receptor complex plays a bigger role in CSL activity in females than males. Thus, GBX would have a greater effect on CSL activity in females.

**Methods:** Adult (60 days) male and female Sprague-Dawley rats were monitored for 65 min. using a Versamax Activity Monitor containing a Plexiglas box (42x42x30 cm, no bedding). After assessing baseline locomotor activity (15 min), we injected rats with GBX (1.25, 2.5 or 5mg/kg i.p.) (Exp 1) or DZ (1.2 or 2.4 mg/kg) (Exp 2) or vehicle and returned them to the Plexiglas box (Exp 1 = 10 min, Exp 2 = 40 min). All rats were then injected with cocaine (15 mg/kg) and returned to the box for a final locomotor assessment (40 min).

**Results:** Females were more responsive to cocaine than males ( $p=.05$ ). GBX administration at 1.25 mg/kg did not dampen CSL activity in males, but in females, GBX decreased locomotion. At 2.5 and 5 mg/kg, GBX did not alter locomotor activity in either sex. There were also sex differences in response to DZ; low dose (1.2 mg/kg) decreased locomotion in males but not in females, and high dose (2.4 mg/kg) decreased locomotion in females alone.

**Conclusions:** Sex differences in response to these two drugs illustrate differences in the roles of GABAA receptor complexes in the regulation of CSL behavior.

**Support:** DA - 10990

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**A MENTAL ARITHMETIC STRESSOR INCREASES ANXIETY AND HEART RATE BUT NOT CRAVING IN METHAMPHETAMINE-DEPENDENT SUBJECTS.**

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**Aims:** We hypothesized that a novel difficult mental math task (MMT) with financial incentives would increase methamphetamine (MA) dependent subjects' anxiety, craving, and heart rate (HR) and that the task could be used repeatedly to induce stress.

**Methods:** 42 MA dependent individuals completed 2 MMT sessions on different days. HR, anxiety, and craving were measured immediately before (baseline) and after (post) the MMT and, again, 5 minutes later. Anxiety and craving were measured with 100 point visual analog scales. The MMT consisted of five minutes of serial subtraction with difficulty changed at the beginning of each minute based on performance; there were 100 total subtractions. The salience of the MMT was increased by subtracting \$0.50 (from an initial \$50 payment) for each incorrect answer.

**Results:** MMT increased anxiety and HR. There were main effects of time for anxiety ( $F(2,205)=27.3$ ,  $p<0.0001$ ) and HR ( $F(2,195)=18.2$ ,  $p<0.0001$ ). There were significant differences between baseline and post anxiety levels for both Sessions one (27.9 vs. 45.4, respectively,  $p<0.001$ ) and two (28.9 vs. 40.5, respectively,  $p<0.001$ ). Mean HR increase was 7.2 bpm ( $p=0.027$ ) in Session two, while there was a trend (4.9 bpm,  $p=0.094$ ) in Session one. There were no significant differences between Session one to Session two at the post time points for Anxiety or HR. There was no main effect of time for craving and there were no main effects of session.

**Conclusions:** The MMT can be used repeatedly to induce stress. While the MMT increased subjective and biological markers of stress, it did not increase MA craving. This lack of induced craving in this study differs from past studies examining stress responsivity in users of alcohol and cocaine. Further research should study the relationship between stress and craving in MA users.

**Support:** DA018179

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**ACCESS 2008: PRELIMINARY RESULTS FROM A CLINICAL TRIAL TO ASSESS, STRATIFY, AND MONITOR THE RISK OF PRESCRIPTION OPIOID ABUSE AND MISUSE IN THE PRIMARY CARE SETTING.**

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**Aims:** Evaluate effectiveness and safety of once-daily AVINZA® (morphine sulfate extended-release) and the potential for prescription opioid abuse and misuse (POAM) for up to 4 months in a primary care setting.

**Methods:** ACCESS 2008 is an open-label trial of >1,540 chronic pain patients. Primary care investigators (n=268) used King's Abuse Intervention Regimen (KAIR<sup>SM</sup>) program that provided initial and ongoing assessment of POAM risk, risk stratification, and appropriate interventions. Seven tools, including a treatment agreement, SOAPP-R®, and qualitative urine drug screen [UDS], were used to assign risk level and appropriate interventions. Opioid-tolerant patients with unacceptable opioid side effects or opioid-naïve patients (pain score  $\geq 4/11$ -pt scale) were recruited; ibuprofen or acetaminophen was used for breakthrough pain.

**Results:** The safety population at the preliminary data review (n=1,450) was primarily female (57%), white (87%), 40-69 years of age (71%), and reported musculoskeletal (69%), osteoarthritis (25%), and/or neuropathic (23%) pain, most (92%) for >1 yr. Comorbid psychiatric illnesses were common (depression, 43%; anxiety/panic disorder, 30%). Baseline UDS showed that ~80% of patients tested positive for opioids and 38% tested positive for illicit substances; 52% had a SOAPP-R® score of 10-21 (moderate level of risk). Of investigators completing the trial at the preliminary data review, the majority found the KAIR<sup>SM</sup> tools useful/very useful and ~66% reported plans to continue using the treatment agreement and UDS. Almost 90% of completed patients were satisfied with KAIR<sup>SM</sup>.

**Conclusions:** Preliminary results suggest the use of a combination of clinical tools and stratification may help to assess and monitor the risk of POAM in the primary care setting.

**Support:** King Pharmaceuticals®, Inc.

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**RANDOMIZED, DOUBLE-BLIND TRIAL EVALUATING BUPRENORPHINE TAPER FOR PRESCRIPTION OPIOID ABUSE.**

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**Aims:** Despite recent increases in prescription opioid (PO) abuse, little is known about effective treatments. While long-term maintenance may be warranted, opioid detoxification is worth exploring as some PO users may be less severe than heroin users and also may avoid maintenance therapies due to the stigma associated with them. In this ongoing trial, we aim to evaluate a randomized, double-blind buprenorphine taper for treating PO abuse.

**Methods:** PO-dependent outpatients receive brief buprenorphine stabilization and random assignment to a 1-, 2- or 4-week taper. Those who successfully taper are inducted onto oral naltrexone. All subjects receive double-blind medication administration, behavioral therapy and urinalysis testing throughout the 12-week study.

**Results:** Thus far, 41 PO abusers have participated (26 yrs, 91% Caucasian, 40% female). Participants report using oxycodone as the primary drug, intranasal as primary route and on average 110 mg/day. During stabilization, approximately 75% of urines test opioid-negative. Abstinence declines across all groups during the taper, with steepest declines evident in the 1-week group. By Week 6, 22%, 44% and 44% of subjects in the 1-, 2- and 4-week groups, respectively, are retained, opioid-abstinent and on naltrexone. By Week 12, 0%, 33% and 38% of subjects in the 1-, 2- and 4-week groups, respectively, remain opioid abstinent. Data from the full sample will be presented in June, as well as an examination of baseline demographic and drug use characteristics which may predict treatment response.

**Conclusions:** Preliminary data suggest that a taper may be effective for some PO abusers, with longer-duration tapers appearing to produce more favorable outcomes. It is important to know if a meaningful subset of PO abusers may not require long-term maintenance, especially for younger and/or less severe patients. However, these data also suggest that the majority of PO abusers do not respond to a brief taper and thus may require longer-term maintenance treatments.

**Support:** Supported by NIDA grants R01 DA019989 and T32 DA007242.

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**GAMMA-HYDROXYBUTYRIC ACID IMPAIRS SPATIAL MEMORY AND ALTERS NMDA RECEPTOR SUBUNITS IN ADOLESCENT FEMALE RATS.**

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**Aims:** Gamma-hydroxybutyric acid (GHB) use is prevalent among adolescents and young adults. It is used for its euphoric, sedative/hypnotic and anabolic effects, and in most cases the subject reports of amnesia. Whether GHB affects cognitive functioning in female adolescent rats remains unknown. In this study, effects of GHB exposure on spatial learning and memory in adolescent female rats were tested, and the role of N-methyl-D-aspartate receptor in GHB-induced behavioral effects was investigated.

**Methods:** Adolescent female rats were treated daily with a single injection of GHB for several days, and were tested in the Morris water maze 30 min following the drug administration. Control rats received equivalent volumes of saline. Rats were sacrificed, their hippocampi dissected and frozen immediately. Western blot analyses were carried out for specific NR subunit proteins in control and experimental brain region.

**Results:** Compared to control rats, GHB-treated rats took significantly longer and swam greater distances to find the hidden platform. Specific NR subunit levels were altered following subchronic GHB treatment.

**Conclusions:** Together, these data indicate that GHB exposure in adolescent female rats negatively impacts spatial learning and this may be associated with altered regulation of the N-methyl-D-aspartate receptor.

**Support:** Supported by NIDA (DA-018234)

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**A POTENTIAL METHOD FOR EXAMINING THE STIMULUS PROPERTIES OF DRUGS UNDER CONDITIONS COMPARABLE TO THOSE USED WITH EXTEROCEPTIVE STIMULI.**

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**Aims:** Although operant stimulus control by exteroceptive stimuli is often examined using a procedure in which responding is reinforced in the presence of one stimulus, and extinguished in the presence of another, there are difficulties in using such a procedure when investigating the stimulus properties of drugs. Since the amount of stimulus control by a particular stimulus is assessed by rate of response, the fact that drugs may alter response rates - by mechanisms other than by exerting stimulus control - is troublesome. The research reported here is concerned with the possibility of developing a procedure in which the stimulus properties of drugs can be separated from their direct rate-altering effects.

**Methods:** As a proof of concept, four male, Sprague-Dawley rats were food-restricted and trained to press two levers in a standard operant chamber. Responding on one lever (i.e. the "drug lever") resulted in food delivery according to a random-interval 2.0 min schedule only when cocaine (10.0 mg/kg) was administered, but responding on the other lever (i.e. the "reference lever") was always reinforced according to the same schedule.

**Results:** In three of four rats, rate of responding on the drug lever following drug administration/rate of responding on the drug lever following saline administration was larger than the ratio observed for such rates on the reference lever. Significantly, the ratio of drug to saline rates of response on the drug lever (when it was illuminated) was larger than the ratio of drug to saline rates of response on the reference lever (when it was not illuminated) even though absolute rates of response following saline administration were comparable under these conditions.

**Conclusions:** The method described above could potentially be used to examine the stimulus properties of drugs under conditions more comparable to how exteroceptive stimuli are examined.

**Support:** Supported by NIH R01DA023938.

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**PROBLEM GAMBLING AND RISK BEHAVIOR: RESULTS FROM A BASELINE STUDY AT THE UNIVERSITY OF IOWA.**

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**Aims:** This study aimed to explore associations between problem gambling and high risk behaviors at the University of Iowa, where students engage in high risk behaviors (74.9% (n=353) were found to binge drink in 2003) and a nearby casino recently opened.

**Methods:** Ten gambling-related items taken from two previously validated screening tools, the South Oaks Gambling Screen and the Lie/Bet Screening Tool, were included in a student health survey. The response rate was 96%. Chi-square tests were used to test association between indicators of problem gambling and risk behaviors.

**Results:** Risk behaviors found to be associated with indicators of problem gambling included: number of cigarettes smoked during the last 30 days ( $\chi^2(2)=18.097$ ;  $p=0.000$ ), use of alcohol more than 6 times within the last 30 days ( $\chi^2(1)=3.930$ ;  $p=0.047$ ), use of marijuana more than 6 times within the last 30 days ( $\chi^2(1)=8.362$ ;  $p=0.004$ ), engaging in unintended or regretted sex after drinking ( $\chi^2(1)=9.652$ ;  $p=0.002$ ), the number of sex partners within the last 12 months ( $\chi^2(2)=4.578$ ;  $p=0.101$ ), injuring others after drinking ( $\chi^2(1)=6.899$ ;  $p=0.009$ ), damaging property after drinking ( $\chi^2(1)=9.949$ ;  $p=0.002$ ), using cocaine ( $\chi^2(1)=8.166$ ;  $p=0.004$ ), using chewing tobacco ( $\chi^2(1)=7.621$ ;  $p=0.006$ ), and using Adderall/Ritalin without a prescription ( $\chi^2(1)=9.872$ ;  $p=0.002$ ).

**Conclusions:** These results support the findings of previous studies that indicate a relationship between problem gambling and high risk behaviors. In the future, a longitudinal study will be conducted to determine the nature of these relationships.

**Support:** Problem gambling has been associated with greater use of tobacco and alcohol, greater binge drinking, heavier use of other drugs, use of marijuana and illicit drugs and participation in unprotected sex (LaBrie et al, 2003).

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**EPIDEMIOLOGY OF SUBSTANCE USE DISORDERS IN AUSTRALIA: FINDINGS FROM THE 2007 NATIONAL SURVEY OF MENTAL HEALTH AND WELLBEING.**

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**Aims:** To present preliminary descriptive findings from the 2nd Australian NSMWHB on the epidemiology of substance use disorders. This will include the prevalence of substance use disorders, comorbidity between substance use disorders and mental disorders as well as service use and suicidality amongst those with a substance use disorder.

**Methods:** The 2nd Australian NSMWHB was carried out between August and December 2007. Data were collected via computerized personal interview using the World Mental Health Survey Initiative version of the Composite International Diagnostic Interview (WMH-CIDI). An extended service utilisation module assessed the extent of consultation with a range of health professionals and touched on aspects of pathways to care for people with substance use and mental disorders.

**Results:** One in every four Australians has met criteria for a substance use disorder at some time in their lives (one in twenty in the previous 12 months). Substance use disorders concentrate in young males. Comorbidity between substance use disorders and mental disorders is common and leads to significant disability. A significant percentage of those with substance use disorders display suicidal behaviours.

**Conclusions:** The results of the 2nd Australian NSMWHB will be discussed both as a snapshot of the mental health of Australians circa 2007 as well as in the context of the international epidemiology of substance use disorders.

**Support:** This project was funded by Australian Government Department of Health and Ageing.

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**TROUBLED PARENTS, MOTIVATED ADOLESCENTS: PREDICTING MOTIVATION TO CHANGE SUBSTANCE USE AMONG RUNAWAYS.**

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**Aims:** Overall, research has focused on increasing the level of motivation for change among those seeking substance abuse treatment but it is evident that predictors of motivation are not yet clearly understood, especially among adolescents. The present study examined motivation to change substance use among runaway adolescents who often report more severe substance use, mental health and family problems than non-runaways. Using both primary caretakers' (PCs') and adolescents' reports (controlling for gender and ethnicity), it was expected that the perceived family environment would influence adolescent's motivation to change, but that the influence would be mediated by the level of the adolescents' and PCs' depressive symptoms and substance use.

**Methods:** Participants, 140 parent-child pairs, were involved in an ongoing clinical trial examining substance abuse treatment outcomes among shelter-recruited runaway adolescents and their PCs. Adolescents were between the ages of 12 to 17 years and met DSM-IV criteria for substance abuse or dependence.

**Results:** We estimated two structural equation models to test the relationships among family variables, substance use and depression, and motivation to change. As predicted, for both adolescents and PCs, a negative perspective of the family environment predicted more depressive symptoms which, in turn, predicted higher adolescent motivation to change drug and alcohol use, respectively.

**Conclusions:** This study uniquely contributes to prior research by examining the contribution of family environment characteristics, from both the adolescent and PC report, to understanding adolescent motivation to change. Adolescents are more dependent upon their parents than are most adults for whom motivational interventions were developed. The current study's findings suggest that the family environment and parent behaviors influence adolescent's motivation to change; parent involvement in motivational interventions might be a very fruitful addition.

**Support:** NIDA grant DA016603

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**SPATIAL ANALYSIS OF INJECTION DRUG USE, DRUG TREATMENT, AND HIV IN BALTIMORE CITY.**

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**Aims:** Current estimates suggest that 10% of Baltimore city's population or 60,000 residents are addicted to some form of drugs and are in need of treatment. In 2005, 37% of the prevalent HIV cases and 44% of the AIDS cases in Maryland were attributable to injection drug use (AIDS Administration). In Baltimore city, injection drug use as a route of HIV transmission constitutes the single largest defined group with HIV infection. In response to the association between injection drug use and HIV transmission, Baltimore city started a needle exchange program in 1994 (AIDS Administration). Overall, research has found that needle exchange programs have been effective in reducing the likelihood of needle sharing and transmission of HIV (Bluthenthal, 2000; Gibson, 2000; Monterroso, 2000). Budgetary limitations require that needle exchange sites in Baltimore are placed in areas where the dollar is best spent: the nexus between places where people use, where HIV incidence is an issue, and where treatment portals do not already exist. This research aimed to identify geographic locations with relatively unmet treatment need.

**Methods:** ArcGIS 9.0 zip code data on prevalence and incidence of HIV from the Maryland AIDS Administration were triangulated with evidence of injection drug use (vials, vial caps, and syringes) from the Neighborhood Inventory for Environmental Typology (NIfETy) method (Furr-Holden et. al, 2008), and current needle exchange and drug treatment locations from the Maryland Drug and Alcohol Abuse's online database.

**Results:** Locations with unmet treatment need are identified by areas formed with triangular spatial data. The area under the curve represents the extents of treatment needs in Baltimore City.

**Conclusions:** This research provides a model for informing allocation of drug treatment/HIV prevention resources, especially in cities where mobile drug treatment/HIV prevention portals are an option.

**Support:** This study is supported by National Institute on Alcohol Abuse and Alcoholism, Centers for Disease Control and the Center for the Prevention of Youth violence.

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**EFFECTS OF SIGNALLED DELAYS, DELAY ORDER, AND D-AMPHETAMINE ON DELAY DISCOUNTING.**

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**Aims:** Delay-discounting functions may be obtained within session by assessing choice between a delayed, larger reinforcer and an immediate, smaller reinforcer. Repeating the same delay context (e.g., ascending delays) in a discrete-choice paradigm, however, may lead to a perseverative response pattern when rats are used as subjects. One aim was to increase the variability in delay order (i.e., ascending and descending delays) in an attempt to reduce a perseverative response pattern and gain tighter control over choice by reinforcer amount and delay. A second aim was to assess effects of signaled and unsignaled delays and d-amphetamine on delay-discounting functions.

**Methods:** Subjects: 16 Sprague-Dawley rats. Apparatus: Standard operant-conditioning chambers. Procedure: A discrete-trials procedure, which consisted of choices between a smaller (one pellet), immediate reinforcer and a larger (three pellets), delayed reinforcer. Delays to the larger reinforcer either increased or decreased within session. For one group, delays to reinforcer delivery were differentially signaled by a flashing houselight and for another group the delays were unsignaled. Effects of d-amphetamine on choice were evaluated in both groups.

**Results:** Similar rates of delay discounting and area under the curve (AUC) were observed with ascending and descending delay orders and with signaled and unsignaled delays to reinforcement. Increasing variability in delay order resulted in differences in the choice pattern during 0-s probe sessions in which the larger reinforcer delay was always 0 s. d-Amphetamine had little or no effect on AUC at low doses, but significantly decreased AUC at the highest doses tested, i.e., 1.0 and 1.7 mg/kg.

**Conclusions:** Variable training led to changes in the response pattern during 0-s probe sessions, and choice was sensitive to changes in delay order (i.e., delay discounting was observed with ascending and descending delays). No differential effect of a signaled delay was observed after d-amphetamine administration, which may have disrupted discrimination of the different food amounts at the higher doses.

**Support:** WVU Psychology Department Alumni Fund Grant

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**THERE IS NO WINDOW OF OPPORTUNITY: PREGNANCY AND DISPARITIES IN TREATMENT NEED VS. RECEIPT.**

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**Aims:** To determine if, among those who have used either alcohol or illicit substances in the past month, pregnant women are more likely than non-pregnant reproductive age women to need and to receive treatment for their use. Does pregnancy help or hinder a woman's ability to receive treatment for her substance use?

**Methods:** We used the National Survey on Drug Use and Health (NSDUH) public use data files from 2002 – 2006. NSDUH is an annual survey designed to collect information on substance use prevalence. We computed weighted frequencies of demographic characteristics of current drug and alcohol users stratified by pregnancy status. We computed both crude and adjusted odd ratios (OR) with 95% confidence intervals (CI) using logistic regression to determine predictors of both treatment need and treatment receipt.

**Results:** Pregnant women who used alcohol or illicit substances in the past month were 93% more likely (OR: 1.93, 95% CI: 1.48, 2.52) to be in need of treatment than their non-pregnant counterparts. After adjustment, need for substance treatment was higher among those women who were young (less than 20), white, unmarried, and with less than a high school diploma. However, of those women who needed treatment, pregnant women were not more likely to receive it (OR: 0.89 95% CI: 0.53, 1.50). Receipt of treatment was least likely among those women were employed, married, with at least a high school diploma, and between 21 – 25 years old.

**Conclusions:** Although pregnant women are more likely to need treatment for substance use, they are not more likely than non-pregnant women to receive treatment. Given that treatment in pregnancy improves birth outcomes, this disparity is troublesome. More efforts should be made by clinicians and policy makers to ensure adequate treatment for substance use in pregnancy.

**Support:** None

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**URBAN-RURAL DIFFERENCES IN RISK AND PROTECTIVE FACTORS FOR YOUTH ABUSE OF OPIOID ANALGESICS.**

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**Aims:** To determine whether observed variation in youth opioid analgesic abuse in urban v. rural communities is associated with differences in operant risk and protective factors.

**Methods:** Data were from the public use file of the 2006 NSDUH, a national survey of individuals 12+ years. Urban was defined as a Census Bureau statistical area (CBSA) with 1 million+ pop.; Rural as a non-CBSA. Dependent variables were nonmedical use (NMU) of OxyContin® and "Vicodin®, Lortab® or Lorcet®" ("HC/APAP"). Risk factors: Ease of obtaining marijuana and cocaine, ever approached by a drug dealer, and frequent drinking and marijuana use by school peers. Protective factors: Drug abuse prevention messages (non-school), and parental checking on homework. N=18,222 12-17 year olds. Analysis: Cross-tabulations and logistic regression.

**Results:** Lifetime OxyContin® and HC/APAP NMU were 1.1% and 4.7% respectively in urban, v. 2.3% and 5.9% respectively in rural areas. For rural youth, the odds of nonmedical use (NMU) of HC/APAP were heightened if it was easy to obtain marijuana (OR=12.3) or cocaine (OR=1.98), if youth had been approached by a drug dealer (OR=8.3), and if youth's peers were frequent drinkers (OR=3.1) or marijuana users (OR=5.9). Odds of NMU were 63% lower if parents checked on homework, and 51% lower if youth had seen drug abuse prevention messages outside of school. For urban youth, the odds of HC/APAP NMU were associated with the same factors except for drug abuse prevention messages (NS). For both rural and urban youth, factors affecting the odds of OxyContin® NMU were similar in type but of mostly greater magnitude than those for HC/APAP NMU. Exposure to drug prevention messages outside of school was associated with a 50% lower likelihood of OxyContin® NMU for urban, and 40% lower likelihood for rural youth).

**Conclusions:** Type and magnitude of risk and protective factors varied between rural v. urbanized communities and were associated in expected ways with likelihood of youth opioid analgesic abuse.

**Support:** Abbott Laboratories

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**TELLING THE WHOLE TRUTH AND NOTHING BUT THE TRUTH: RELATIONSHIP BETWEEN SELF-REPORT MEASURES OF DRUG USE AND URINE/HAIR ASSAY RESULTS IN POST-PARTUM WOMEN.**

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**Aims:** While the Drug Abuse Screening Test (DAST) is commonly used to identify persons with drug problems in both clinical and research settings, little is known about DAST scores and objective measures of substance use. Specifically, since the DAST focuses on consequences of drug use, it may not be an effective tool for detecting drug use itself (which may or may not meet criteria for a substance use disorder). The purpose of this study was to examine the predictive utility of the DAST-10 and compare it to a more parsimonious approach for identifying drug use (e.g., questions about frequency of recent drug use using items from the WHO Alcohol, Smoking, and Substance Involvement Screening Test [ASSIST]).

**Methods:** The sample consisted of 180 low-income, primarily African-American post-partum women recruited in-hospital post-delivery. All women first provided informed consent to complete an anonymous, computerized assessment battery which included the DAST-10 and ASSIST. Thereafter, they consented to provide urine and hair samples for drug assay. For objective measures, women were categorized drug positive if hair or urine samples tested positive for drug use. For the computerized ASSIST self-report measure, a woman was classified drug positive if she reported any use of opiates, amphetamines, marijuana or cocaine in the 3 mos prior to becoming pregnant. For the DAST, a cumulative score >1 was considered positive for drug problems.

**Results:** The simple screener derived from the ASSIST outperformed the DAST in sensitivity (.61 vs .47) and area under the curve (.72 vs. .63) even when the lowest possible DAST cutoff (scores of 1 and higher) was used.

**Conclusions:** Study findings suggest that although the DAST may be good at detecting individuals with a drug use disorder, a single question of drug use was a better predictor of at-risk women.

**Support:** Research was supported by NIH grants NIDA R21 DA018975 and NCMHD P60 MD002256.

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**AEROBIC EXERCISE ATTENUATES THE ESCALATION OF COCAINE INTAKE UNDER EXTENDED-ACCESS CONDITIONS.**

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**Aims:** When laboratory animals are permitted to self-administer cocaine under extended-access conditions, they progressively escalate their drug intake in a manner similar to that observed in human substance-abusing populations. We have previously reported that aerobic exercise decreases cocaine self-administration under short-access conditions, but the effects of exercise on measures of drug self-administration under long-access conditions are not currently known. The purpose of the present study was to determine whether exercise attenuates the escalation of cocaine intake in rats self-administering cocaine during daily 6-hour test sessions.

**Methods:** Female Long-Evans rats were obtained at weaning and divided into two groups immediately upon arrival. Sedentary rats were housed individually in standard laboratory cages that allowed no exercise beyond normal cage ambulation. Exercising rats were housed individually in modified cages with running wheels affixed to the interior of the cage. After 6 weeks under these conditions, rats were surgically implanted with venous catheters and trained to self-administer cocaine under a fixed ratio (FR) schedule of reinforcement during daily 2-hour training sessions. Once responding stabilized, sessions were increased to 6 hours and the escalation of cocaine intake was examined over 14 consecutive days.

**Results:** Sedentary and exercising rats did not differ in cocaine intake during the initial 2-hour training sessions or during the first 6-hour test session. Both groups exhibited significant increases in cocaine intake over the next 13 extended-access sessions, but this effect was significantly greater in sedentary rats than exercising rats.

**Conclusions:** These data indicate that aerobic exercise attenuates the escalation of cocaine intake under extended-access conditions and suggest that physical activity may be an effective intervention in the prevention of substance abuse disorders.

**Support:** This study was supported by NIDA Grant DA14255.

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**DIFFERENCES IN BRAIN ACTIVATION BETWEEN MARIJUANA SMOKERS AND NON-SMOKING CONTROLS DURING A SPATIAL NAVIGATION FMRI TASK.**

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**Aims:** Animal studies have demonstrated cannabinoid-related impairments in spatial memory and hippocampal function, which may result due to a high density of cannabinoid receptors in this region. The objective of this study was to examine fMRI BOLD signal during the performance of a hippocampus-mediated spatial navigation task in current marijuana smokers (MJ; n=5) and non-using control subjects (n=7).

**Methods:** Imaging data were acquired on a 3.0 Tesla Siemens MRI scanner, motion corrected, and analyzed in SPM5. fMRI BOLD data were collected while subjects performed a computerized virtual analogue of the Morris water maze task, which included 2 conditions: retrieval (locating a hidden platform) and non-mnemonic control (navigate to a visible platform). Subjects were pre-trained (learning phase) on the task offline prior to imaging.

**Results:** During the learning phase, MJ smokers demonstrated shorter latencies to first movement, however no other significant performance differences were detected between controls and MJ smokers. During the retrieval condition, MJ smokers had a longer path to find the hidden platform than control subjects. No group differences were observed for the visible platform condition. Data from BOLD fMRI scanning showed that non-using controls exhibited greater activation than marijuana smokers of key areas involved in spatial processing, including the hippocampus and parahippocampal gyrus during retrieval versus control condition.

**Conclusions:** Overall, MJ smokers exhibit hypoactivity in the hippocampal/parahippocampal area during spatial navigation. Given the paucity of data on visuospatial memory function in cannabis users, these findings contribute to our understanding of the neural changes underlying marijuana use and the impact of its use on learning and memory.

**Support:** R03DA022482-01A2(Sneider, JT); DA020269-01 (Yurgelun-Todd, DA)



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### A COMPARISON OF THREE METHODS FOR TRAINING SOUTH AFRICAN SUBSTANCE ABUSE COUNSELORS IN COGNITIVE BEHAVIORAL THERAPY.

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**Aims:** Stimulant dependence is a concern in South Africa due to its relationship with risky sexual behavior and increased HIV/AIDS rates. Cognitive behavioral therapy (CBT) is an empirically supported treatment for stimulant dependence. Yet, little is known about the most effective and efficient way of training counselors in CBT. This study aims to evaluate three models for training South African counselors in CBT skills and the relationship between training model, counselor self-efficacy, and self-report of CBT skill implementation. We hypothesize that the two experimental groups will report greater self-confidence and skill implementation compared to the control condition.

**Methods:** The study consists of 119 counselors randomly assigned to: 1) in-vivo training, 2) distance learning training, and 3) manual-only training. Data are collected at baseline, 4-, 8-, and 12-weeks and again at 24-weeks post training.

**Results:** Counselor confidence in ability to implement CBT techniques did not differ between groups at baseline,  $F(2, 116) = 1.76, p = .18$ . Self-report of CBT skill implementation over the 12 weeks of the study differed between groups,  $F(2, 103) = 10.63, p < .001$ , with in-vivo ( $M = 3.36, SD = 0.44$ ) and distance learning ( $M = 3.58, SD = 0.53$ ) groups reporting higher levels of skill implementation compared to the manual only group ( $M = 3.01, SD = 0.54$ ). In-vivo and distance learning groups did not differ from each other. Further, confidence in counselor's ability to implement CBT at baseline was correlated with self-report of skill implementation for the in-vivo (Pearson  $r = .40, p = .01$ ) and distance learning (Pearson  $r = .43, p = .01$ ) groups, but not for the manual-only group (Pearson  $r = .06, p = .75$ ).

**Conclusions:** These findings suggest that counselors prefer a more in-depth training model for learning CBT skills, and that both in-person and distance trainings appear to foster self-efficacy that translates into greater self-report of skill implementation.

**Support:** NIDA R01 DA019063-01A1

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### THE USE OF ACAMPROSATE VS PLACEBO IN ALCOHOLICS WITH COMORBID ANXIETY OR DEPRESSION.

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**Aims:** There have been numerous studies evaluating the use of acamprosate in the treatment of alcohol dependence. However, to date, there are no studies evaluating acamprosate in alcoholics with comorbid anxiety or depression. The current study is a placebo-controlled, multi-site, trial of acamprosate in the treatment of alcoholics with comorbid anxiety or depression.

**Methods:** Participants were seen weekly for 12 weeks. Substance use and psychiatric diagnoses were determined by the MINI International Neuropsychiatric Interview. Alcohol use was assessed using the TimeLine Follow-back as well as breathalyzer readings. Pertinent assessments include: Montgomery Asberg Depression Rating Scale (MADRS), and the Hamilton Anxiety Rating Scale.

**Results:** 243 individuals were screened and 90 (55 M, 35 F) were randomized, with an equal distribution of acamprosate and placebo. All met criteria for alcohol dependence, and 93.3% ( $n=84$ ) had major depression. The majority of participants ( $n=64$ ) had lifetime comorbid generalized anxiety disorder. There were no statistically significant differences in demographics between groups. The average age was 44.1 (9.3) years; mean years of education was 13.5 (2.6) and the majority of participants were Caucasian (72.2%;  $n=69$ ) and employed (62.2%;  $n=56$ ). Baseline average drinks per drinking day was slightly higher in the acamprosate group compared to placebo (11.2 (6.6) vs. 8.4 (4.9);  $p<0.05$ ). Study medication was well tolerated in both groups. Although no statistically significant differences were found, drinking decreased over time in both groups. No differences were found in symptoms of anxiety or depression between groups at baseline or during treatment.

**Conclusions:** This study did not find acamprosate to be more beneficial than placebo in decreasing alcohol use in a group of individuals with anxiety and depression. The use of acamprosate did not appear to worsen psychiatric symptoms. Data from the current trial are similar to other recent studies on acamprosate.

**Support:** This study was sponsored by Forest Laboratories

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### SEX DIFFERENCES IN RESPONSE TO INTRAVENOUS NICOTINE IN SMOKERS.

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**Aims:** Although approximately 45 percent of smokers in the US are women, the influence of sex on nicotine dependence remains incompletely understood. Evidence from preclinical and clinical studies indicates that there are significant sex differences in nicotine's effects. The goal of this study was to determine if men and women differ in their acute response to intravenous (IV) nicotine, which has not been examined in previous studies.

**Methods:** Participants were 12 female and 12 male non-treatment seeking smokers. The data presented were collected during the adaptation session of 2 two human laboratory nicotine studies. Participants were instructed not to smoke after midnight on the adaptation day, thus remaining abstinent for 8 hours before presenting at the laboratory at 8 AM. Approximately, 45 minutes after an IV catheter placement, baseline measurements were obtained and participants were given saline followed by 2 escalating doses of nicotine (0.5 and 1.0 mg/70 kg) intravenously.

**Results:** In response to nicotine, women compared to men, had enhanced ratings for "drug strength," "head rush," and "bad effects." Women also had enhanced suppression of smoking urges by nicotine as assessed by the Brief Questionnaire on Smoking Urges (BQSU). Nicotine-induced heart rate as well as systolic and diastolic blood pressure increases were similar in magnitude in men and women.

**Conclusions:** Our findings, consistent with several previous studies, support greater sensitivity of female smokers to some of the subjective effects of nicotine, including reduced urge to smoke. Further studies are warranted to examine the role of this differential nicotine sensitivity to development of nicotine dependence and response to nicotine replacement treatments in men and women.

**Support:** This research was supported by the Veterans Administration Mental Illness Research, Education and Clinical Center (MIRECC) and the National Institute on Drug Abuse grant R01-DA 14537. The authors were supported by career development awards, K02-DA021304 (MS) and K01-DA-019446 (MM).

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### HIV PREVENTION IN PROBLEM-SOLVING COURTS: A REVIEW.

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**Aims:** We review scientific literature addressing HIV prevention research in problem-solving court settings, such as drug and mental health courts. Currently there are more than 1,500 problem solving courts in the United States offering treatment alternatives to defendants in the criminal justice system. Applying behavioral principles, they use both rewards and sanctions to modify behaviors. These courts can be powerful tools for preventing HIV infection. They can directly prevent HIV transmission by sanctioning drug use and encouraging participation in addiction treatment. Indirectly, they can prevent HIV by serving as a platform for prevention services, such as HIV testing and counseling, psycho-educational interventions, and linkage to medical care.

We searched the relevant English-language literature from 1993-2008 using databases such as PubMed, examining keywords and authors known to have conducted research in the area.

**Conclusions:** The research literature shows little evidence that HIV-prevention approaches have salience in the operation of problem-solving courts. Numerous evidence-based approaches have been developed for participants in substance abuse and psychiatric treatment settings, but these have seldom been applied to problem-solving courts. Some demonstrations have indicated that HIV-prevention activities can be integrated into problem-solving courts, with impact on both patients and the court system. Yet well-controlled research has seldom been attempted in these settings, and research findings to date are scarce. Future research can take advantage of this under-explored opportunity to prevent HIV infection and to adapt well-tested, effective interventions to the problem-court setting.

**Support:** R21DA020369, U10DA015815, P50DA09253, 5T32MH018261

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### NIDA'S CLINICAL TRIALS NETWORK DELIVERS EVIDENCE-BASED TREATMENTS THROUGH COMPARATIVE EFFECTIVENESS RESEARCH.

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**Aims:** The National Institute on Drug Abuse established the CTN in 1999 as the home for comparative effectiveness research to validate and compare science-based addiction treatments. The scientifically-derived findings of CTN trials guide community-based drug treatment clinicians to make better treatment decisions.

The CTN brings together practitioners from community-based drug abuse treatment programs and scientists from university-based research centers in an alliance that fosters communication and collaboration. This alliance facilitates the development and implementation of evidence-based treatments in community practice clinics, raising the quality of addiction treatment throughout the nation.

Two projects are presented to illustrate how CTN accomplishes "Comparative Effectiveness Research":

#### Project 1 Opioid Detoxification

Opioid dependent individuals seeking short term treatment were given either the standard-of-care drug clonidine or the new drug product buprenorphine/naloxone (BUP/NX) in a 13-day detoxification program.

BUP/NX was found to be 3-5 times more effective than clonidine in detoxifying patients. Most patients treated with clonidine did not complete the program, but nearly all the BUP/NX patients completed.

#### Project 2 Motivational Incentives

The effectiveness of a low-cost prize-based contingency management treatment was added to routine care in community outpatient psychosocial clinics and methadone maintenance clinics. Treatment seeking drug abusers were randomized to routine care with or without motivational incentives during a 12 week trial.

Motivational incentives increased the number of patients attending scheduled treatment sessions and led to better treatment outcomes.

**Conclusions:** These findings have been packaged into comprehensive training and treatment tools for use by practitioners throughout the country. The packages continue to inform the drug abuse treatment field about the evidence-based superiority of BUP/NX over clonidine in short-term detoxification and the value of low-cost motivational incentives.

**Support:** NIDA

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### PREDICTORS OF RISKY SEXUAL BEHAVIOR IN INCARCERATED DRUG USERS IN SRI LANKA.

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**Aims:** The number of illicit drug users in Sri Lanka has been growing over the last decade. Polydrug use is common with heroin and cannabis being the main drugs of abuse. Risky sexual behavior among drug users is a major concern due to the spread of HIV and hepatitis. Aim of the study is to ascertain predictors of risky sexual behavior amongst drug users.

**Methods:** A structured questionnaire was administered by interviewers to 278 Sinhalese-speaking male prisoners charged with illicit drug use who fulfilled DSM-IV criteria for substance dependence. Participants also completed the AUDIT, Severity of Dependence Scale (SDS) and personality trait measures: Zuckerman Sensation-Seeking Scales, Behavioral Inhibition System/Behavioral Activation System (BIS/BAS) and Sensitivity to Punishment/Sensitivity to Reward Questionnaire (SPSRQ). Selected demographic, father's drug-use pattern, intravenous (IV) and polydrug use, childhood sexual abuse, AUDIT, SDS and personality scores were analyzed using backward multivariate logistic regression to predict sexual promiscuity, sex with commercial sex workers (CSW) and homosexual behavior.

**Results:** The age of initiation of sexual behavior were significantly younger in the drug users who had risky sexual behaviors. IV and polydrug use, AUDIT and SDS scores, low educational background, sensation-seeking personality traits were predictors of sexual promiscuity and sex with CSW. Predictors of homosexual behavior included paternal and IV drug use and sensitive to punishment personality scores.

**Conclusions:** Consistent with previous studies, IV and polydrug use are predictors of unsafe sexual behavior among drug users. Impulsive personality traits were also shown to be associated with risky sexual behavior amongst drug users. Early screening for these risk factors and sex education programs at an early age could be a useful preventative measure.

**Support:** LO Dissabandara was supported by Health Group scholarship from Griffith University

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### DOES PRESCRIPTION DRUG ABUSE TAKE A HOLIDAY?

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**Aims:** Abuse and misuse of prescription drugs (APD) is a significant problem in the US. Understanding associated behavioral factors may help in treatment or education efforts. While holidays have an important impact on social behavior, limited data exist on whether changes in behavior for holidays include temporal changes in APD. We analyzed intentional exposures during holiday periods (HP) using RADARS® System Poison Center (PC) data.

**Methods:** Spontaneous calls from the public and healthcare professionals are recorded by PC using a standardized, electronic data collection system. APD data for the following prescription drugs (PD) were analyzed: methadone, hydrocodone, oxycodone, morphine, fentanyl, buprenorphine and oxycodone. Daily APD case count from 43 PC for 8 HP (HP = day before, holiday, and day after) in 2003 -2007 were compared to the annual mean case count ( $\pm 1$  [1SD] and 2 standard deviations [2SD]). The holidays analyzed were 4 family-gathering holidays (Thanksgiving, Christmas, Mother's day and Valentine's day) and 4 party/social-gathering holidays (July 4th, Memorial day, Labor day and New year's eve).

**Results:** The daily APD case count was normally distributed. Over the study period 25 of 120 HP showed a decrease of at least 1 SD from the mean ( $p > 0.05$ ) and 9 of 120 HP showed an increase of at least 1 SD from the mean ( $p > 0.05$ ). 6 HP showed a change of greater than 2 SD from the mean, with 4 days increased and 2 days decreased. All 4 days with an increase of  $> 2SD$  occurred during the New Years HP. However the change for the New Year's HP was not consistent, with 5 days showing an increase, 3 showing a decrease of at least 1 SD and 7 showing no significant change from the mean. Analysis of all 8 holidays showed no significant difference when evaluating day prior, day of, or day post holiday.

**Conclusions:** The prevalence of APD was not impacted by the occurrence of 8 traditional holidays. Additionally the type of holiday did not have an impact on APD.

**Support:** Support for this study was provided by RADARS System.

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### NEIGHBORHOOD FACTORS PREDICTING TREATMENT COMPLIANCE AND REHOSPITALIZATION FOR Dually DIAGNOSED PATIENTS.

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**Aims:** The purpose of this study was to investigate what neighborhood and individual factors of dually diagnosed patients discharged from acute inpatient care predict: (1) initial outpatient treatment attendance, and (2)rehospitalization within one year.

**Methods:** Geographic Information Systems (GIS) technology and stepwise-forward logistic regression modeling were utilized on data extracted from the medical records of 380 patients diagnosed with co-morbid mental health and substance use disorders discharged from an acute psychiatric inpatient unit in Philadelphia, PA. Geographic data on the neighborhood environment were obtained from public sources.

**Results:** Returning home, living in areas with high vacant housing rates and relatively far from an AA meeting place, having a chief complaint of bizarre behavior, and a urine drug screen positive for heroin, decreased the likelihood of showing up for initial outpatient treatment following psychiatric hospitalization. The likelihood of being rehospitalized within a year was greater for Hispanic patients, and for those patients who had at least one prior admission and who lived close to the nearest NA meeting. Patients living in areas with a higher educational attainment had a reduced likelihood of rehospitalization

**Conclusions:** A more explicit focus on the individual's neighborhood and community context represents an important but under-studied area for psychiatry, both in terms of research and clinical practice, which can potentially enhance long term care and treatment planning for psychiatric patients. Future research is needed to better understand the influence of the neighborhood environment to help predict important clinical outcomes

**Support:** Supported in part by grants from Temple University's Institute for Policy Affairs, the College of Liberal Arts (CLA) Research Incentive Fund, and the College of Liberal Arts Mid-Career Fellowship Award.

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**EXPLORING NEO PERSONALITY FACTORS IN METHADONE MAINTENANCE TREATMENT PATIENTS.**

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**Aims:** Many methadone maintenance treatment (MMT) patients report dissatisfaction with treatment; it is possible that personality traits may influence subjective effects of methadone during the trough condition. We compared personality profiles of MMT patients to normative data and assessed the influence of personality on trough subjective responses to methadone.

**Methods:** Patient responses to the NEO Personality Inventory – Revised were compared to normative data and grouped based on differences in mean dimension scores. Patient responses to the Addiction Research Center Inventory (ARCI), Profile of Mood States (POMS), and Subjective Opiate Withdrawal Scale (SubOWS) at trough condition were compared amongst groups.

**Results:** Ninety MMT patients (53M:37F, 40±8 years, on a dose of 85±44mg of methadone for 8±11 months and in treatment for 65±47 months) completed the study. Compared to the normal score of 50, MMT patients scored higher on the neuroticism (59.8±11.1) and lower on the agreeableness (42.7±10.9) and conscientiousness (38.7±10.1) dimensions. Subjects in the high neuroticism (n=53) and low conscientiousness (n=57) groups scored higher on the SubOWS (17.2±10.5 vs. 11.8±9.9, p=0.016 and 17.3±10.5 vs. 10.9±9.5, p=0.005, respectively) and on measures of negative ARCI and POMS subscales (e.g., dysphoria: 3.2±2.0 vs. 1.8±1.9, p=0.001 and 3.1±2.1 vs. 1.9±1.8, p=0.008; depression/dejection: 20.9±13.2 vs. 7.8±9.7, p<0.001 and 18.8±13.3 vs. 9.8±11.8, p=0.002) compared to those with normal scores. Subjects in the low agreeableness group (n=41) scored higher on the POMS measure of anger/hostility (11.9±8.9 vs. 6.9±6.3, p=0.002) compared to those with normal scores.

**Conclusions:** Personality factors are associated with different subjective responses to measures of mood, perceived withdrawal symptoms and drug effect at trough methadone condition.

**Support:** Internal funding.

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**RELATIONSHIP INFLUENCE AND HIV RISK BEHAVIOR AMONG RE-ENTERING WOMEN OFFENDERS.**

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**Aims:** Studies have shown that relationships with parents, peers, and partners can be related to risk and protective factors for women offenders. This study will examine the positive and negative influences of parents, peers, and partners as risk and protective factors for women prisoners preparing for community re-entry to better understand their HIV risk behavior, including risky sex and risky drug use.

**Methods:** The study includes cross-sectional data from women offenders enrolled in three protocols of the NIDA funded Criminal Justice Drug Abuse Treatment Studies (CJDATS) cooperative agreement. Permission to use data from each protocol was granted by the Lead Center PI. In each study, baseline interviews were completed with incarcerated women during the final months of their sentence who were preparing for community re-entry. Relationship influences were categorized as "positive" (example - enjoyed being together) or "negative" (example - getting into arguments or big fights) for women offenders based on behaviors during the year prior to incarceration. HIV risk behaviors were categorized as risky drug use and risky sexual activity.

**Results:** Multivariate regression models suggested that positive parental influence was associated with reduced HIV risk (b=-0.10, p=0.023) and reduced drug use in the past 6 months (OR=0.53, p=0.005). However, negative peer influence increases drug use including both risky needle behavior (OR=1.37, p=0.032) and any drug use in past 6 months (OR=1.63, p=0.033).

**Conclusions:** These data suggest that, while relationships are generally important to women, particular types of positive or negative relationship influences may be protective for engaging in HIV risk behavior. Implications for targeting re-entry interventions for women offenders will be discussed.

**Support:** NIDA 5U01DA016205

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**ENRICHMENT-INDUCED DIFFERENCES IN NICOTINE DRUG DISCRIMINATION IN RATS IS NICOTINIC RECEPTOR MEDIATED.**

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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 alters the discriminative stimulus effects of nicotine using an operant drug-discrimination procedure.

**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 6:00-19:00 hr. EC and IC rats were trained on a two lever operant procedure to discriminate 0.3 mg/kg (s.c.) nicotine from saline. Either saline or nicotine injections were administered using a two day alternating dosing regimen 15 min. prior to the 15-min. drug-discrimination session. Following acquisition of the discrimination (80% appropriate responding) a nicotine generalization curve (0.03-0.3 mg/kg) was determined. Following completion of the nicotine generalization curve, pretreatments with either the nicotinic antagonist mecamylamine (0.0625-1.0 mg/kg) or the dopamine D2 antagonist eticlopride (0.01-0.3 mg/kg) were administered prior to injections of the nicotine training dose. Following the antagonist pretreatments brains were collected for autoradiography in order to determine nicotinic receptor density in mesolimbic brain regions.

**Results:** Both EC and IC rats acquired nicotine drug discrimination. Although, EC rats were less sensitive to the discriminative stimulus effects of lower nicotine doses compared to IC rats. There was also differential sensitivity between EC and IC rats in response to pretreatments with mecamylamine, but not eticlopride. [125I]Epibatidine binding in coronal sections suggest differences in nicotinic receptor density in mesolimbic regions from EC versus IC brains.

**Conclusions:** These results suggest that environmental enrichment decreases sensitivity to the discriminative effects of nicotine potentially through changes in the nicotinic receptor.

**Support:** This research was supported by the Creighton University College of Arts and Sciences

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**DELAYED DISCOUNTING AND QUESTIONNAIRE MEASURES OF IMPULSIVE AND INATTENTIVE BEHAVIORS ARE HETEROGENEOUS.**

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**Aims:** Delayed discounting (DD) is typically conceptualized as a measure of impulsive choice behavior. In preparation for genotype/phenotype association analyses, we have examined several phenotyping measures of impulsive and inattentive behavior to determine their discriminant validity.

**Methods:** Factor analysis using Varimax rotation (SPSS v.16) was used to analyze data from 81 opioid-dependent participants collected during screening for inpatient research studies. Here, we report only measures that had factor loadings of at least +/-0.3.

**Results:** DD of heroin, using a normally distributed AUC measure across relatively short delay intervals (3, 6, 12, 24, 48, 72 and 96 hr), was significantly greater during hypothetically imagined heroin-withdrawal vs. -satiated conditions, F(1, 80)=82.86, p<0.001. The Impulsive Relapse Questionnaire (IRQ) measures tendencies toward impulsive drug relapse and has 5 subscales. DD and two IRQ subscales, Motor Speed and Control Deficit, positively loaded on factor 2. Unexpectedly, the IRQ Capacity for Delay subscale did not load on the DD factor. The Stanford Time Perception Inventory (STPI), a questionnaire that measures time horizons and insensitivity to future consequences, has been previously found to differentiate drug- and non-drug dependent individuals. Our analysis showed that less STPI Future Orientation, and greater Present Hedonism and Present Fatalism scale scores loaded on the same factor (factor 1) as adult ADHD symptoms (measured with the Assessment of Hyperactivity and Attention (AHA), IRQ Control Deficit and current IV heroin use. AHA total child and total adult symptom scores both loaded on factor 5.

**Conclusions:** These factor analysis results provide discriminative validity that questionnaire measures of impulsive and inattentive behaviors are heterogeneous with DD scores.

**Support:** NIH R01 DA015462 and Joe Young, Sr. Funds (State of Michigan)

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### FUNCTIONAL MRI OF METHAMPHETAMINE USERS USING A GO NO-GO TASK.

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**Aims:** Methamphetamine (Meth) is a major stimulant abused in the United States. A better understanding of the neuronal circuitry involved in addiction may lead to more effective treatments. This study examines the brain circuitry in Meth users and controls with a "go no-go" (GNG) paradigm using blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI).

**Methods:** Currently eleven Meth abstinent subjects, and eight controls have been enrolled from a targeted enrollment of 30 per group. Each subject had an fMRI scan while performing three GNG trials of four minutes each on a 3 Tesla MRI scanner. A multi-echo spiral sequence capable of acquiring data from the whole brain every two seconds with reduced susceptibility artifacts and improved BOLD contrast was used. The GNG task requires that the subject press a button every time any letter appears ("go") except for the letter "X" (a "no-go") at a rate of one letter per second. Each four minute run contained approximately twenty no-goes.

**Results:** Brain activation correlated with the successful no-goes was observed within a network involving response inhibition and attention in both Meth users and control subjects (including the ventral lateral prefrontal cortex, anterior cingulate cortex, insula, and the dorsolateral prefrontal cortex). The Meth users appeared to have more intense activation. Meth users show greater activation in the insula as well as the anterior cingulate cortex ( $P$ -corrected $<0.03$ ).

**Conclusions:** The preliminary result of greater activation during the GNG task in the Meth users suggests that Meth use might lead to injury in the inhibitory circuit in the brain and may reflect a compensatory neural process.

**Support:** Supported by NINDS/NIDA (U54NS056883 for the Specialized Neuroscience Research Program), NIDA (K02 DA020569 for AS, K24DA016170 for LC) and NCCR (G12 RR003061 for the RCMI and P20 RR11091 for the RCMI-CRC).

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### DO ORGANIZATIONAL PROCESS IMPROVEMENT INTERVENTIONS SIGNIFICANTLY CHANGE MOTIVATIONAL INTERVIEWING KNOWLEDGE, ATTITUDES, AND USE BY SUBSTANCE ABUSE TREATMENT COUNSELORS?

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**Aims:** The Texas Process and Practice Improvement Study determined if use of motivational interviewing (MI) by treatment counselors was influenced by two interventions: quarterly feedback on client outcomes and a change workshop to improve organizational factors affecting MI use.

**Methods:** Participants included counselors ( $n=148$ ) in 32 substance abuse treatment clinics randomized to receive interventions. Surveys were administered at pre and post-study and included subscales on MI Perceived Knowledge, Training Participation, Skepticism, Usefulness, Research Awareness & Support. Independent  $t$ -tests were used to assess if significant differences existed in counselor pre to post-study MI subscale scores depending on the interventions received.

**Results:** Significant differences were demonstrated on some MI subscales. Counselors in the Graphic Feedback+MI reported lower MI Perceived Knowledge ( $t(29)=-.953$ ,  $p=.045$ ), higher MI Training, and lower MI Skepticism ( $t(29)=.551$ ,  $p=.013$ ). Counselors in the Graphic Feedback+Change Workshop+MI Training reported lower MI Perceived Knowledge ( $t(47)=1.34$ ,  $p=.010$ ) and higher MI Training ( $t(45)=-3.90$ ,  $p=.001$ ). Counselors in the Graphic Feedback reported higher MI Training ( $p=.001$ ) and counselors in No Intervention group reported lower MI Perceived Knowledge ( $p=.033$ ) and higher MI Training ( $p=.005$ ) while No Intervention Group 2 demonstrated no significant change. Counselors in all groups demonstrated no significant change on MI Usefulness, Research Awareness, or Support.

**Conclusions:** Initial analysis reveals that interventions do influence counselors' knowledge of and training in MI but not always in the hypothesized direction. Counselors in no intervention clinics demonstrated no significant change on MI subscales, while counselors in clinics receiving more interventions and MI training report less perceived knowledge of MI but less skepticism of MI use.

**Support:** DHHS Grant No. 1R21DA019759-01 through contract with the Texas Department of State Health Services

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### THE SPECIAL CASE OF THE *MU* OPIOID RECEPTOR AND THE EVOLUTION OF THE OPIOID RECEPTOR FAMILY.

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**Aims:** The aim of this study was to investigate the evolution of vertebrate opioid receptors and to compare opioid receptors from different classes of vertebrates.

**Methods:** Methods used included cloning opioid receptor cDNA from amphibian brain tissue, expressing cloned human and amphibian *mu* opioid receptors in CHO cells for comparative binding studies, and bioinformatics.

**Results:** The results yielded three main findings: 1) The sequences of *mu*, *delta*, and *kappa* opioid receptors were more identical with each other in the earlier-evolved species (fish, newt, and frog) than in the mammalian and human species. This finding highlights the discovery that opioid receptor types are diverging with vertebrate evolution, so that each type of receptor becomes more distinct. 2) When the amino acid sequences of the four types of opioid receptors were lined up using bioinformatics, a pattern emerged such that the *mu* and *delta* receptors were most related to each other, and the *kappa* and nociceptin receptor to each other. This pattern suggests that the evolution of opioid receptor proteins arose by a single opioid receptor gene (the unreceptor), which was duplicated twice to give four types of opioid receptor genes. 3) The *mu* opioid receptor underwent similar natural selection pressures in all animals as it is the most conserved of the four types. Additional data show that the *mu* opioid receptor exhibits the greatest rate of change of the four types. Natural selection of vertebrate opioid receptors led to a *mu* opioid receptor that is more effective at producing opioid effects, such as analgesia. Unfortunately, this also means that the evolution of opioid receptors has produced a *mu* opioid receptor in humans that is more likely to cause opioid substance abuse and dependence.

**Conclusions:** These studies show that there is an evolutionary vector of opioid receptor divergence leading to greater type-selectivity in humans, that the four types of vertebrate opioid receptors arose by two whole genome duplication events, and that the *mu* opioid receptor shows evidence of the most rapid adaptive evolution.

**Support:** Supported by NIH-NIDA grant DA012448 to CWS

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### CHARACTERISTICS ASSOCIATED WITH COCAINE USE IN PREGNANT OPIOID-DEPENDENT WOMEN: PRELIMINARY RESULTS FROM THE MATERNAL OPIOID TREATMENT, HUMAN EXPERIMENTAL RESEARCH STUDY.

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**Aims:** To compare the baseline characteristics of cocaine-using and non-cocaine-using women screened for participation in the MOTHER study, a multi-site double blind, double dummy clinical trial to examine the safety and efficacy of buprenorphine vs. methadone in opioid dependent pregnant women.

**Methods:** Of 1038 women consented and screened for inclusion, 436 used cocaine and 602 did not. These two groups were compared on demographic and other characteristics, including treatment history, other substance use, legal, psychiatric, and medical problems and Addiction Severity Index (ASI) measures.

**Results:** Women with cocaine use compared to women who did not use cocaine were older (30.05 versus 26.66 years,  $p=.000$ ), more likely African American (35.3% vs. 8.6%,  $p=.000$ ) and less likely to be married (8.0% vs. 13.1%,  $p=.013$ ); Treatment history differed between groups: cocaine users had higher numbers of prior methadone treatments (2.27 versus 1.86,  $p=.000$ ) and higher rates of daily opioid use (96.3% versus 75.2%,  $p=.000$ ). Legal problems were higher in cocaine users ( $p=.001$ ). Medically, hepatitis C, but not hepatitis B positive serology was higher in cocaine users (59.7% versus 30.4% in non-users,  $p=.000$ ). ASI composite scores were higher for cocaine using women in the legal ( $p=.002$ ), employment ( $p=.028$ ), drug ( $p=.000$ ), psychiatric ( $p=.030$ ), and family/social ( $p=.000$ ) but not in the medical or alcohol categories.

**Conclusions:** These data show the association of cocaine use with multiple measures of baseline severity in this population and support the importance of studies involving the treatment of pregnant women with co-occurring cocaine use and opioid dependence.

**Support:** NIDA RO1DA 045778 015832 015764 015738 017513 018410 018417 015741

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### OUTCOMES OF A SWISS PRACTITIONER NETWORK SURVEY ON THE CURRENT USE OF U.S. TREATMENT APPROACHES TO COCAINE ADDICTION.

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**Aims:** Most research on pharmacological and psycho-social therapies for cocaine addiction has been undertaken in the U.S. However, not all U.S. treatment approaches are adaptable to Western European countries, e.g. due to differences in health insurance systems. Therefore, the Swiss Cocaine Treatment Glossary (SCTG) project has been launched in 2005 with the objective of developing national treatment guidelines for Switzerland taking account of U.S. treatment approaches to cocaine addiction. The glossary is based on biannual international literature reviews, rated for relevance by an expert group.

**AIM:** To assess the usefulness of the SCTG for practitioners from specialized outpatient facilities in Switzerland.

**Methods:** A questionnaire-survey was conducted, focusing on the use of treatment approaches to cocaine addiction as illustrated in the SCTG to a total of 327 practitioners from specialized outpatient facilities.

**Results:** In general, the SCTG was evaluated positively. The most frequently used psychotherapeutic approaches were those of cognitive-behavioral (51.9%) and systemic therapy orientations (22.1%). Contingency management was not reported at all (0%). However, unlike recent research suggested, the most frequently prescribed pharmaceutical was methylphenidate (32.2%). Modafinil was prescribed in 9.1% of all cases. A combination of cognitive-behavioral therapy and methylphenidate was most commonly used (25.4%).

**Conclusions:** The present survey underlines the usefulness of the SCTG to specialized practitioners. Yet, further adaptations are required, to foster the level of awareness for and the use of the SCTG also among less specialized actors in the field.

**Support:** This study is supported by the Swiss Federal Office of Public Health (FOPH).

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### RELATIVE ABUSE POTENTIAL OF INTRAVENOUS OXYCODONE, HYDROCODONE AND MORPHINE IN NON-DEPENDENT OPIOID ABUSERS.

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**Aims:** Misuse and abuse of prescription opioids is an increasing problem in the United States. Diversion from oral to intravenous administration of these drugs is not uncommon, yet little is known about the relative abuse potential of these drugs when administered intravenously.

**Methods:** This inpatient study employs a double-blind, randomized, within-subject, placebo-controlled design to examine the relative abuse potential of intravenous doses of oxycodone (Napp Pharmaceuticals, Cambridge, United Kingdom), hydrocodone (Abbott GmbH & Co, Ludwigshafen, Germany) and morphine (Amphistar Pharmaceuticals, South El Monte, CA). Six healthy adult volunteers reporting recreational opioid use participated in 11 experimental sessions, including one active practice session. Intravenous doses were infused over 5-min and included three identical active doses of each drug (5 mg up to 20 mg) and saline placebo. Subjective, performance and physiological effects were collected before and for 6 hr after drug administration.

**Results:** All three opioids produced prototypic mu agonist effects (increased ratings of high, good effects and miosis) that were generally dose-related. Active doses produced peak increases in EtCO<sub>2</sub> of approximately 10 mmHG from baseline, generally within 20 minutes of administration. Formal relative potency analyses remain to be conducted, but equipotent increases in visual analog scale and street value ratings were observed across drugs and doses. AUC analyses suggest that the duration of subjective effects of low doses of hydrocodone may be shorter than those of the other two drugs.

**Conclusions:** These three commonly used opioids produce similar prototypical mu opioid effects when administered intravenously, but they appear to have important pharmacodynamic differences that are dependent on dose.

**Support:** Grant R01 DA 016718(SLW)

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### ATTITUDES OF COLLEGE STUDENTS TOWARD USE AND MISUSE OF PSYCHIATRIC MEDICATIONS.

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**Aims:** To examine student attitudes related to use and misuse of psychiatric medications.

**Methods:** Participants were 364 students (60.5% female), aged 18-31. They completed self-report questionnaires including the Day's Mental Illness Stigma Scale (DMISS), which is comprised of 7 subscales (Anxiety, Relationship Disruption, Hygiene, Visibility, Treatability, Professional Efficacy, and Recovery); the Michigan Alcohol Screening Test (MAST); the Drug Abuse Screening Test (DAST); and the Attitudes Toward Psychiatric Medications scale, which has medication Effectiveness and Concern about side effects subscales.

**Results:** Nine students reported being prescribed ADHD medication, but 45 students reported misuse. Ten students reported being prescribed a benzodiazepine, and 12 reported misuse. Fifteen students were prescribed an antidepressant, with only 1 student reporting misuse. MAST scores were highly correlated with DAST scores ( $r = .39, p < .001$ ), but were unrelated to student attitudes. High scores on DMISS Anxiety, Relationship Disruption, and Hygiene were positively related to Concern about side effects ( $r = .19, p < .001$ ;  $r = .15, p < .004$ ;  $r = .15, p < .006$ ). Scores on DMISS Efficacy and Recovery were negatively related to Concern ( $r = -.30, p < .001$ ;  $r = -.25, p < .001$ ) and positively related to Effectiveness ( $r = .24, p < .001$ ;  $r = .23, p < .001$ ). Misuse of ADHD medication was highly correlated with misuse of a benzodiazepine ( $r = .31, p < .001$ ) and negatively correlated with DMISS scores for Anxiety, Relationship Disruption, Hygiene, and Concern ( $r = -.11, p < .04$ ;  $r = -.11, p < .04$ ;  $r = -.13, p < .02$ ;  $r = -.16, p < .002$ ). Misuse of benzodiazepines was negatively correlated with DMISS scores for Anxiety and Relationship Disruption ( $r = -.12, p < .02$ ;  $r = -.11, p < .04$ ).

**Conclusions:** As the stigma surrounding mental illness decreases, the acceptability of taking psychiatric medications may increase. More effort is needed to balance psychoeducation regarding the nature of mental illness and the dangers of misusing psychiatric medications.

**Support:** This study was supported by the University of Florida.

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### CHILDHOOD PREDICTORS OF FIRST CHANCE TO USE AND USE OF CANNABIS BY YOUNG ADULTHOOD.

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**Aims:** To examine prospectively the linkage between childhood antecedents and progression to early cannabis involvement as manifest in first chance to try it and then first onset of cannabis use.

**Methods:** Two consecutive cohorts of children entering first grade of a public school system of a large mid-Atlantic city in the mid 1980s were assessed and then followed into young adulthood (mean age 21) when first chance to try and first use were assessed for 75% of the original sample ( $n=1698$ ). Childhood assessments obtained at entry into first grade included standardized measures of reading and math readiness and teacher ratings of behavioral problems. Child self-reports about depression and anxiety and family characteristics assessed by parental report were obtained in third grade. Regression and time to event models included covariates for gender, race, and family disadvantage.

**Results:** Young adults with aggressive/disruptive behavior problems in first grade were not more likely to ever have had a chance to use cannabis when compared to peers without behavior problems ( $RR=1.5, 95\% CI= 1.0, 2.3, p=.08$ ); however, their first chance to try cannabis occurred at an earlier age (log rank  $p=.001$ ) and they were more likely to smoke cannabis once given the opportunity ( $RR=1.9, 95\% CI=1.3, 2.7, p=.001$ ). Higher school readiness scores were independently associated with increased risk of first chance to smoke cannabis, but these scores did not predict transition from first chance to first use. Childhood emotional feelings were not associated with either first chance to use or cannabis use ( $p>.05$ ).

**Conclusions:** Childhood readiness and behavioral problems may influence the risk for cannabis smoking indirectly via an increased likelihood of first chance to use.

**Support:** Supported by grants MH 71395, DA09897, DA04392, DA019805, and a career development award K05DA015799 (JCA).

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### INDUCTION OF OPIOID-DEPENDENT INDIVIDUALS ONTO BUPRENORPHINE AND BUPRENORPHINE/NALOXONE FILM STRIPS.

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**Aims:** Buprenorphine (B) and buprenorphine/naloxone (B/N) sublingual tablets are effective for opioid dependence treatment. Film strip (FS) formulations of B and B/N are being developed. FSs dissolve faster and provide unit dose child resistant packaging amenable to tracking for diversion and misuse. This study compared the ability of B vs BN FSs to suppress spontaneous opioid withdrawal (w/d) during the first 2 days of a 5 day induction.

**Methods:** Residential, opioid-dependent participants initially maintained on morphine (M) (30 mg SC 4x daily) underwent double blind challenges with IM placebo (P) or N (0.4 mg); subjects who had precipitated w/d with N and not P based upon predefined criteria were randomized to 5 days of double blind B or BN FSs (followed by B tablets). FS doses were split on day 1 (4 or 4/1 mg 3x), and then 16 (or 16/4) mg administered 1x on day 2. The primary outcome measure was total Clinical Opiate Withdrawal Scale (COWS) score; other measures were also assessed.

**Results:** 38 subjects completed the M phase, qualified for FSs, and randomized to B or BN FSs. 4 of the 38 dropped out during FS dosing, typically reporting continued opioid w/d on the first day of FSs. For subjects who completed FS dosing (18 on B and 16 on BN), groups did not differ by mean age (41 yrs), gender or race (74% male, 65% white). There was a significant decrease in COWS scores from baseline (pre-first FS dose) to the peak post-FS dose score, but no significant differences between groups in baseline (B=9.1, BN=10.1) or peak post-FS COWS scores (B=4.2, BN=5.7). A similar pattern was found for other measures associated with opioid w/d. There were no severe adverse events; FSs were generally well tolerated.

**Conclusions:** Results show a B and BN FS formulation can be safely and effectively used in opioid dependence treatment for dose induction, with significant decreases in opioid w/d. There was no evidence of significant differences in efficacy between B and B/N FSs.

**Support:** Supported by a contract from Reckitt Benckiser Pharmaceuticals Inc. and NIDA grants DA08045, DA023186

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### PRESCRIPTION DRUG USE AMONG BABY BOOMERS: INSIGHTS FROM CLINICIAN INTERVIEWS.

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**Aims:** Community recruited Baby Boomers with dependence on four or more drugs were compared with those with three or less drugs.

**Methods:** The NIDA-funded Prescription Drug Misuse, Abuse and Dependence Study is interviewing 400 18 to 65 year olds using a test-retest methodology to determine how reliably these problems are assessed. Two hundred are randomly assigned to a clinician validation assessment; 200 receive a qualitative assessment.

**Results:** Preliminary information suggests that half the sample of 50 to 65 year olds can be categorized as heavily drug dependent while the other half is dependent on less drugs.

To date, the heavily drug dependent group began their misuse of prescription opiates at a mean age of 28 (range of 18 – 38) while those dependent on less drugs began their misuse of prescription opiates at a mean age of 38 (range of 28 - 49). In the case of all drug categories except alcohol and marijuana, the heavily drug dependent were more prevalent among those who used that particular category than those dependent on less drugs. In all cases, the onset of drug use per drug category was earlier for the heavily dependent than those dependent on less drugs.

In terms of mental health comorbidity, major depressive disorder was common in both groups; but no one in the later or less severe drug user group was diagnosed with Antisocial Personality Disorder by the clinicians while the majority of the early and continual users were so diagnosed.

**Conclusions:** Clinicians recording complete mental health and substance abuse histories may capture two different groups of older prescription opiate dependent users. One of these groups is much more likely to be persistently dependent on other substances, including cocaine, and to have more conduct and antisocial behavioral problems. Physicians may be completely unaware of the illicit drug histories of their patients without asking.

**Support:** This work supported by NIDA, R01DA020791, PI Linda B. Cottler, PhD, MPH

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### ARE INJECTION-RELATED RISK BEHAVIORS AND FOOD INSECURITY ASSOCIATED?

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**Aims:** We examine if there is an association between food insecurity and injection-related risk behaviours.

**Methods:** We interviewed 145 injectors in London, ON about injection practices, food insecurity, housing, service use, HIV and hepatitis C status and physical and mental health status. With logistic regression we assessed the association between food security and risk behaviours.

**Results:** In the past 6 months on a daily/weekly basis, 52% did not have enough to eat because of a lack of money; 60% did not eat the quality/quantity of food because of a lack of money; 65% did not eat/drink enough because of an extended drug 'run'; 33% used a food bank. Re-use of equipment varied: 21% re-used a needle, 19% re-used water and 37.3% re-used a cooker and 18% re-used a filter. The odds of re-using needles were increased for those reporting food insecurity (OR=2.7), injecting outdoors (OR=3.7) and HCV positive status (OR=2.9) and reduced for those under age 25 (OR=0.87). For sharing water, the odds were increased for those reporting food insecurity (OR=2.6), HCV positive status (OR=3.2) and opiate injecting (OR=7.0). The odds for cooker re-use were increased for IDUs reporting food insecurity (OR=1.9), injecting outdoors (OR=2.7) and HCV positive status (OR=2.25). For filter re-use, the odds were increased for those reporting food insecurity (OR=3.1), injecting outdoors (OR=6.7) and HCV positive status (OR=3.8).

**Conclusions:** IDUs have frequent experiences of food insecurity which are correlated with risk behaviour and may increase the likelihood of many injection related problems. Addressing food-related needs among IDUs will require stronger ties with social services, food banks and shelters and address issues of stigma to ensure IDUs have access to these programs.

**Support:** Canadian Institutes of Health Research

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### SEX DIFFERENCES IN APPROACH-AVOIDANCE BEHAVIOR IN THE RUNWAY MODEL OF COCAINE SELF-ADMINISTRATION.

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**Aims:** Evidence from both human and animal studies suggests that males and females differ qualitatively and quantitatively in their cocaine self-administration. While men are more likely to abuse the drug, women show a faster transition from initial use to treatment-seeking and are more prone to relapse. The current study was devised to assess whether such differences might stem in part from the differential impact in males and females of cocaine's well-known mixed rewarding and anxiogenic effects. Previous work by our group has employed a runway model of drug self-administration that is sensitive to both the positive and negative properties of cocaine. In this model, male rats develop over trials a distinct pattern of "approach-avoidance" conflict about entering a goal box for cocaine (but not for other reinforcers). The current project examined whether or not there are sex differences in this approach-avoidance behavior during runway IV cocaine self-administration.

**Methods:** Male and female rats were trained to traverse the runway once a day (for 21 days) for a single 1.0 mg/kg IV infusion of cocaine delivered upon goal box entry. The time to leave the start box (start latency), to run the alley and enter the goal box (run time) and the numbers of stop-and-retreat conflict responses (retreats) were recorded on every trial.

**Results:** Consistent with prior studies, males exhibited a progressive increase in run time and numbers of retreats across trials. However, in contrast to males, females exhibited significantly shorter run times and fewer retreats.

**Conclusions:** These data suggest that female rats exhibit a lower ambivalence about entering a cocaine-paired environment and are more motivated to seek cocaine than male rats, which may contribute to sex differences in addiction vulnerability.

**Support:** This work was supported by grants from NARSAD (TEK) and NIDA (DA21161 to TEK and DA05041 to AE).

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**POOR FRONTO-LIMBIC CONNECTIVITY: A BRAIN ENDOPHENOTYPE FOR RAPID RELAPSE TO COCAINE?**

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**Aims:** We recently showed that a behavioral phenotype of rapid relapse (i.e., relapse by week 2 in outpatient treatment) was characteristic of cocaine patients who had not achieved cocaine-free urine status during screening period. We hypothesized that relapse-prone cocaine patients may have compromised brain function: A deficit in frontal modulation of downstream limbic systems. On the basis of cocaine urine status (positive, CocPos vs. negative, CocNeg) at screening, we examined the differences in functional amygdala connectivity during resting, non-drug video, and cocaine video conditions.

**Methods:** Nineteen cocaine dependent patients (CocPos=11; CocNeg=8) were scanned after 7 days in a controlled therapeutic setting to ensure stable, cocaine-free state. ASL (arterial spin-labeled) perfusion fMRI at 3 Tesla was used to measure rCBF under the following conditions: 1) Resting; 2) Non-drug video; 3) Cocaine videos while attempting to i) increase and ii) decrease subjective craving. Perfusion data were pre-processed within SPM2, using functional connectivity analyses with amygdala (AMYG) as the reference region.

**Results:** Functional connectivity analyses (cluster-corrected whole brain) revealed a striking absence of frontal-AMYG connectivity in CocPos during all conditions (Pcorrected<0.001; cluster size => 20 contiguous voxels). In contrast, frontal regions (e.g., genu anterior cingulate) maintained good AMYG connectivity in CocNeg, even during Rest. When attempting to inhibit cocaine craving, CocNeg showed inverse connectivity between dorsal cortical regions and AMYG; this pattern was entirely absent in CocPos, showing only strong intra-limbic connectivity with AMYG.

**Conclusions:** Poor connectivity between frontal modulatory regions and AMYG may be the brain endophenotype underlying CocPos' difficulties in resisting cocaine use. Impaired fronto-limbic connectivity may provide an important marker of greater relapse vulnerability in clinical trials, and a critical treatment target for interventions.

**Support:** NIDA (RO1-DA10241/DA15149; P60-DA05186; P50-DA12756); VA MIRECC

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**BEHAVIORAL NALTREXONE THERAPY PLUS DEPOT NALTREXONE FOR HEROIN DEPENDENCE: A RANDOMIZED CONTROLLED TRIAL.**

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**Aims:** Poor adherence and high attrition have undermined the effectiveness of naltrexone as a treatment for opioid dependence. The goals of this project were to improve retention on oral naltrexone treatment among opioid-dependent patients by examining (1) the effect of an intensive behavioral therapy model (Behavioral Naltrexone Therapy) compared to a Compliance Enhancement (CE) control condition intended to simulate standard practice and control for attention; and (2) to test the effect of a single dose of long-acting injectable depot naltrexone prior to discharge from hospital, compared to placebo.

**Methods:** Opioid-dependent patients were admitted to hospital for detoxification and induction onto oral naltrexone, then randomized (N=89) in a 2-by-2 design to receive either BNT or CE, and to receive a dose of either active or placebo depot naltrexone injection (Depotrex, BIOTEK) prior to discharge from hospital. BNT combines voucher incentives, motivational interviewing, cognitive behavioral relapse prevention, and significant other monitoring of medication ingestion, in an effort to reduce non-adherence and attrition. All patients were maintained on oral naltrexone throughout the 6-month trial.

**Results:** Retention in treatment at study end point (6 months) was highest in the group that received intensive behavioral therapy plus active depot naltrexone injection prior to discharge (BNT + depot group) (11/23, 48%), followed by BNT + placebo (5/21, 24%), control therapy (CE) + depot (4/24, 17%), and CE + placebo (3/21, 14%) (chi-square (3 d.f.) = 8.36, p < .05).

**Conclusions:** The findings suggest that a combination of intensive behavioral therapy and long-acting injectable depot naltrexone shows promise for improving the effectiveness and viability of naltrexone as a treatment for opioid dependence.

**Support:** Supported by R01 DA010746 and K24 DA022412.

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**HIV SEXUAL RISK BEHAVIORS AND PHYSICIAN SCREENING IN OFFICE-BASED BUPRENORPHINE TREATMENT.**

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**Aims:** Opioid dependent patients receiving office-based buprenorphine may exhibit HIV sexual risk. Our prior work demonstrates that sexual risk may not change during buprenorphine treatment. Our aim was to examine the change in patients' sexual risk behaviors during buprenorphine treatment and providers' sexual risk screening practices.

**Methods:** In phase I we conducted an audio computer-assisted self-interview survey of patients receiving buprenorphine in a community practice. Patients described their pre-treatment and in treatment behaviors along with their physicians' sexual risk screening. In the phase II we conducted a national survey of buprenorphine prescribers regarding their sexual risk screening.

**Results:** 80 patients, ranging in age from 18-62 years responded: 77% male, 94% Caucasian, 57% reported primarily prescription opioid use, 18% reported current injection drug use. Compared to pre-treatment behavior, in treatment behavior was: had sex (67% vs. 64%, p=.74), mean number of sexual partners (0.9 vs. 0.8, p=.15), mean number of unprotected sex episodes (6.4 vs. 4.0, p=.06), and the mean number of sex episodes while high (4.4 vs. 0.8, p<.001). Patients reported that buprenorphine had affected their sexual risk in the following way: no change (72%), decreased (15%), increased (1%). Patients reported that their buprenorphine prescribers infrequently discussed: HIV testing (55%), sexual behaviors (55%), condom use (32%), negotiating safer sex (26%), or risk of multiple partners (34%). HIV testing was performed 25% of the time. 376 buprenorphine providers responded to the survey. They reported discussing: HIV testing (55%), sexual behavior (45%), condom use (30%), negotiating safer sex (25%), or risk of multiple partners (32%). HIV testing was performed by 33% of providers.

**Conclusions:** Discussions about HIV testing and sexual risk are infrequent despite ongoing risk. Strategies are needed to refine and increase HIV counseling and testing among patients receiving office-based buprenorphine to meet current national guidelines.

**Support:** The Robert Wood Johnson Foundation and NIDA grants: K12 DA00167, R01 DA019511, K24 DA00445

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**DISTINCT MECHANISM OF METHAMPHETAMINE- AND METHYLPHENIDATE-INDUCED DOPAMINE-RELATED NEUROTOXICITY.**

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**Aims:** Methamphetamine (METH) is a powerfully addictive psychostimulant that dramatically affects the mammalian central nervous system. Methylphenidate (MPH) has been shown to have psychostimulus effects similar to METH. In the present study, we, however, explored the differences between METH and MPH.

**Methods:** Male BALB/c mice were repeatedly treated with METH (16 mg/kg, s.c.), MPH (80 mg/kg, s.c.) or saline four times with 2 hr intervals. These treatments caused self-injured behaviors with different patterns, but eventually these behaviors were disappeared within 2 hr after every treatment. Twenty four hr after the last injection, we performed Western blotting assay to measure the levels of phosphorelated tyrosine hydroxylase (p-TH), dopamine transporter (DAT), glial fibrillary acidic protein (GFAP)-positive astrocyte and ionized calcium-binding adaptor molecule 1 (Iba1)-positive microglia.

**Results:** As a result, repeated METH treatment caused a significant decrease in levels of p-TH (p<0.001 vs. saline treatment) and DAT (p<0.001 vs. saline treatment), and a significant increase in levels of GFAP (p<0.001 vs. saline treatment) and Iba1 (p<0.005 vs. saline treatment) in the mouse striatum tissue compared to saline treatment. In contrast, MPH had no such a decrease or increase in the expression levels of p-TH, DAT, GFAP and Iba1.

**Conclusions:** The present study provides the novel evidence for the distinct mechanisms between METH and MPH on dopamine-related neurotoxicity.

**Support:** The Research Grant (19A-2) for Nervous and Mental Disorders from the Ministry of Health, Labour and Welfare

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# ROLE OF DORSAL HIPPOCAMPUS AND ROSTRAL BASOLATERAL AMYGDALA IN COCAINE CUE EXTINCTION LEARNING.

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**Aims:** The dorsal hippocampus (DH) and basolateral amygdala (BLA) are integral substrates for extinction of fear-salient cues. Given that the DH connects reciprocally with the rostral BLA (rBLA), we hypothesized that both rBLA and DH may be important substrates for cocaine cue extinction learning.

**Methods:** Rats were trained in 1-hr sessions to self-administer 1 mg/kg cocaine under a second-order reinforcement schedule with discrete light and contextual sound cue presentations. Rats then underwent 2 weeks of daily 1-hr abstinence sessions (cocaine, cues and levers not present), followed by two 1-hr extinction sessions (no cocaine, but cues and levers present). Rats (n=6-8) received an infusion of lidocaine (100 µg) or vehicle bilaterally into the rBLA or DH, or asymmetrically into the rBLA and contralateral DH prior to extinction sessions.

**Results:** Bilateral inactivation of DH slowed cocaine cue extinction learning. From day 1 to 2 of extinction training, there was a large decrease in responses after vehicle, while responses did not change much after lidocaine. Change in responses between days 1 and 2 was smaller after lidocaine than after vehicle (p<0.04). Bilateral inactivation of rBLA did not slow extinction learning. Both vehicle and lidocaine groups had equally large decreases in responses from day 1 to 2. However, asymmetric inactivation of rBLA and DH slowed cocaine cue extinction learning (p<0.005), similar to bilateral DH inactivation.

**Conclusions:** Findings suggest a role for DH in early cocaine cue extinction learning. Since rBLA inactivation alone was unable to slow extinction learning, disruptive effects of asymmetrical inactivation may reflect either a cooperative memory system interaction or an effect of unilateral DH inactivation. However, as the rBLA exerts a modulatory influence over DH learning functions, asymmetric inactivation of these sites may produce effects early in cocaine cue extinction learning that are not predicted by inactivation of each site alone due to an imbalance in bilateral hippocampus function following asymmetric inactivation.

**Support:** Supported by DA11716

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# ADDICTION TO FOOD: POTENTIAL USE OF 18-METHOXYCORONARIDINE TO TREAT OBESITY.

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**Aims:** Aims: It has become increasingly apparent that there is significant overlap between the systems regulating drug reward and food intake. 18-Methoxycoronaridine (18-MC), a selective antagonist of alpha3beta4 nicotinic receptors, has been previously shown to reduce the self-administration of several drugs of abuse and reduce operant responding for sucrose in rats. The aim of these studies was to examine the effects of 18-MC on intake of palatable substances and the development of obesity in rats.

**Methods:** Methods: Female and male Sprague-Dawley rats (250-275g) were used in sucrose-induced and high-fat diet-induced models of obesity.

**Results:** Results: In the present experiments the acute administration of 18-MC (10-40 mg/kg i.p.) reduced ad libitum ingestion of sucrose (5%) and saccharin (0.1%). Furthermore, the acute administration of 18-MC (20 mg/kg i.p.) also blocked ghrelin-induced increases in sucrose intake. In rats having unlimited access to sucrose (30 %), chronic treatment with 18-MC (20 mg/kg i.p.) prevented sucrose-induced increases in body weight, decreased fat deposition, and reduced consumption of sucrose while not altering food intake. In rats consuming a high fat diet, 18-MC (20 mg/kg i.p. for 14 days) reduced weight gain and fat deposition.

**Conclusions:** Conclusions: These data suggest that alpha3beta4 nicotinic receptors may participate in maintaining obesity and ghrelin-mediated feeding behavior, possibly becoming a new and important target for anti-obesity agents.

**Support:** Support: DA 016283.

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# MODAFINIL BLOCKS MORPHINE-PRIMED REINSTATEMENT OF CONDITIONED PLACE PREFERENCE.

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**Aims:** Opiate addiction is a chronic disorder characterized by high rates of relapse following long periods of abstinence. This problem requires new relapse-prevention treatments that do not have abuse potential. Recently, a few clinical trials have shown that wake-promoting agent modafinil is effective in treating cocaine dependence. We investigated the effects of systemic modafinil pretreatment on drug-primed reinstatement of extinguished morphine conditioned place preference (CPP), as an animal model of relapse to drug-seeking, and also examined the possible involvement of metabotropic glutamate (mGlu) II/III receptors.

**Methods:** Place preference for morphine (8 mg/kg, ip) was induced in male Sprague-Dawley rats (n=7-12 for each experimental group). Following extinction training, CPP was reinstated by a morphine priming injection (8 or 16 mg/kg). Effects of modafinil (100 and 300 mg/kg, ip) pretreatment were investigated on reinstatement of morphine CPP.

**Results:** We found that pairing of modafinil (300 mg/kg) with an environment during conditioning did not induce CPP (P>0.05); and did not alter the expression of morphine CPP in the presence or absence of morphine 8 mg/kg (P>0.05). While modafinil (300 mg/kg) pretreatment by itself does not cause reinstatement, pretreatment of rats with modafinil 300 mg/kg - but not 100 mg/kg - thirty min prior to the morphine priming injection completely blocked reinstatement of CPP (P<0.05). We also found that injection of the mGlu II/III antagonist, LY341495 (3 mg/kg), 30 minutes prior to modafinil administration completely reversed the blocking effect of modafinil on reinstatement of morphine CPP (P<0.05).

**Conclusions:** Findings of the current study indicate that modafinil blocks the reinstatement of morphine CPP, an effect that seems to be mediated - at least in part - by mGlu II/III receptors. Our findings suggest modafinil as a potential treatment for prevention of relapse in opiate addiction.

**Support:** This study was supported by PHS grants R01 DA017289, R37 DA06214 and P50 DA015369. Modafinil was generously provided by Cephalon Inc.

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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 for several petitions requesting a change in the control status of nabilone, removal of marijuana and tetrahydrocannabinols (THCs) from schedule I, control of tramadol and propofol, decontrol of sibutramine and 6-beta-naltrexol and amendment to CFR so as to allow generic products of dronabinol in sesame oil into schedule III.

**Results:** DEA is currently reviewing the data for hallucinogens such as 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), 5-methoxy-alpha-methyltryptamine (5-MeO-AMT), 5-methoxy-N,N-diethyltryptamine (5-MeO-DET), 5-methoxy-N-methyl-N-isopropyltryptamine (5-MeO-MIPT), N,N-diisopropyltryptamine (DIPT), 4-hydroxy-N,N-diisopropyltryptamine (4-OH-DIPT), 4-iodo-2,5-dimethoxy-phenethylamine (2C-I), 2,5-dimethoxy-4-ethylthiophenethylamine (2C-T-2), and 2,5-dimethoxy-4-iodoamphetamine (DOI) for possible control under the CSA. Chemical synthesis/pharmacological studies for 2,5-Dimethoxy-4-chloroamphetamine (DOC), 2,5-Dimethoxy-4-chlorophenethylamine (2C-C), 2,5-Dimethoxy-4-methylphenethylamine (2C-D), and 2,5-Dimethoxy-4-ethylphenethylamine (2C-E) are currently ongoing to determine if these substances meet the requirements for possible control under the CSA.

**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.

**Support:** Drug Enforcement Administration



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**MOTIVATION FOR PHYSICAL ACTIVITY AND LEG DISEASE IN METHADONE MAINTENANCE PATIENTS.**

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**Aims:** There is a growing body of research supporting the beneficial effects of regular physical activity/exercise in substance abuse treatment. Low motivation may be a barrier to engaging in physical activity/exercise. Little is known about how leg disease, which is highly prevalent in injection drug users who injected in veins of their legs, might affect motivation for physical activity. In this study, we examined values, attitudes, and beliefs related to motivation for physical activity in a large cross-sectional sample of opioid dependent adults in methadone maintenance treatment (MMT).

**Methods:** Participants (N = 569) were opioid dependent adults in MMT. A stratified, cross sectional design was used. Participants individually completed questionnaires and had their legs evaluated for vein and artery disease. An investigator developed Lifestyle Mobility Questionnaire was used to quantify walking, activity level, participation in sports/exercise and motivation for physical activity.

**Results:** Most walked less than half a mile per day. Few participated in sports. Confirmatory factor analysis showed that the set of attitude, value, and belief items defined a reliable and internally consistent scale. Motivation for physical activity was predictive of daily walking, participation in sports, and maintenance/increase in level of daily activities over the past 5-years. Motivation for physical activity was inversely related to age, years of injection drug use, history of chronic health problems, arterial and venous disease of the legs. Leg disease had a strong negative effect on activity level but did not affect motivation for physical activity. These relationships held up when controlling for age and other covariables in a structural equation model.

**Conclusions:** This pattern of results suggests a potential protective effect of elevated lifetime activity and a bidirectional causal relation between activity and leg disease. MMT patients maintain motivation for physical activity that is not affected by the health conditions of their legs.

**Support:** NINR/NIH), R01 NR009264.

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**SUBSTANCE ABUSE TREATMENT NEEDS, SERVICE UTILIZATION, AND THE ROLE OF CULTURE AMONG AMERICAN INDIANS/ALASKA NATIVES IN RECOVERY: PERSPECTIVES OF CLIENTS AND SERVICE PROVIDERS.**

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**Aims:** This qualitative study explored the substance abuse treatment needs and service utilization, particularly cultural-specific services, among urban American Indian/Alaska Native (AI/AN) clients.

**Methods:** Focus groups were conducted with both clients (in a treatment agency targeting the AI/AN community) and treatment staff serving AI/AN clients (representing 6 agencies). The discussions were audio recorded, transcribed verbatim, and analyzed using ATLAS.ti.

**Results:** The client focus group participants were AI/AN individuals receiving outpatient substance abuse treatment. The majority was male; half were over 21 years old. Clients' lengths of stay in treatment ranged from less than 1 week to more than 9 months. The staff focus group consisted of males and females from outpatient and residential treatment settings. Ages ranged from 26 to 58 years and the majority self-identified as AI. Staff had worked in the substance abuse field between 4 to 22 years and at their current agencies between 7 months to 12 years. Both client and staff participants reported reasons for clients entering treatment (e.g., criminal justice system involvement) and treatment service needs (e.g., counseling, dental) that for the most part were similar to other substance-using populations. However, treatment-related issues and needs that were particularly salient to the AI/AN community were associated with relocation from reservations and multigenerational alcoholism and drug use. In addition, focus group participants indicated that exposure to or relearning about Native culture and traditions may facilitate the recovery process by instilling a positive sense of identity, pride, and connection/reconnection with family and community.

**Conclusions:** Exploratory focus group findings suggest that service providers' cultural sensitivity and culture-specific activities may play a crucial role in maximizing the effect of treatment among AI/AN clients.

**Support:** Supported by: NIDA P30DA016383 and K05DA017648

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**HOW USEFUL IS WHAT WE HAVE? LIMITATIONS OF COCHRANE REVIEWS, THE CASE OF SUBSTANCE TREATMENT IN PREGNANCY.**

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**Aims:** To describe the public health promise and methodological problems of Cochrane reviews.

Cochrane reviews are central to evidence-based medicine. However by focusing exclusively on randomized controlled trials (RCTs) a large swath of the published literature is excluded from their purview. Our experience conducting three of the four published reviews that examined interventions for substance use in pregnancy has brought particular methodological issues to light. Pregnancy is time-limited event and therefore amenable to a RCT intervention. However this study design is employed mostly in academic centers serving poor inner-city women. How useful then is this evidence? We begin with a brief overview of the Cochrane Library with particular emphasis on the addiction and obstetric literature. Then the following methodological topics are addressed: the tensions between clinically useful, clinically expedient, and sociologically meaningful outcomes; the difference between experimental and real world interventions; problems in external validity due to RCT recruitment in pregnancy; and confounding and bias in exposure assignment. We contrast our results from Cochrane reviews with the observational studies that were excluded from our reviews. Finally we argue for a more flexible design for systematic reviews that can allow the inclusion of more diverse study designs. The current Cochrane software (RevMan 5.0) appears to offer hope for this.

**Conclusions:** Pregnancy is a unique moment in a woman's life course where individual motivation for behavioral change is coupled with the availability of social support (such as prenatal care). Furthermore, interventions for drug problems in pregnancy have the possibility of not only improving birth outcomes, but affecting maternal health and child development across the life course. The summary of quality evidence is therefore necessary in the guidance of both clinical medicine and current policy.

**Support:** Part of this study was funded by the Alcohol Education Research Council, UK.

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**PROTECTIVE EFFECTS OF ENVIRONMENTAL ENRICHMENT ON COCAINE-SEEKING BEHAVIOR DURING ABSTINENCE.**

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**Aims:** A problematic characteristic of drug addiction is the high incidence of relapse that occurs following even extended periods of abstinence. Underlying factors that may contribute to relapse are contextual- and cue-elicited craving which sensitize (incubate) during abstinence. Treatments aimed at attenuating the incubation of drug craving may help to prevent relapse. The present study examined the behavioral effects of environmental enrichment (EE) housing during abstinence on subsequent cocaine-seeking behavior upon re-exposure to previously drug-associated cues.

**Methods:** All rats were trained to self-administer cocaine for 15 days while housed in isolate conditions (IC). Each cocaine infusion was accompanied by light/tone cues. Following training, rats were assigned to live in either EE or IC for either 1 or 21 days of abstinence. Subsequently, cocaine-seeking behavior was assessed by placing rats back into the self-administration chamber and recording lever presses that resulted only in presentation of the light/tone drug-paired cues.

**Results:** The results suggest that drug-seeking behavior incubates throughout abstinence, and that EE housing during this time attenuates cocaine-seeking behavior. To determine the neural basis of EE's protective effects, we plan to examine BDNF and ERK levels within several mesolimbic regions.

**Conclusions:** These findings may have important implications for treatments aimed at reducing drug craving.

**Support:** Supported by DA11064, DA023123, and F31DA023746

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**ATTACHMENT AND ALEXITHYMIA IN ALCOHOL MISUSING OUTPATIENTS.**

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**Aims:** Attachment difficulties have been proposed as a key risk for alexithymia, a multifaceted personality trait associated with mood regulation difficulties and alcohol misuse. The present study investigated the relationship between attachment and alexithymia in an alcohol misusing population.

**Methods:** Participants were 146 patients aged between 18 and 70 years undertaking outpatient Cognitive-Behavioural Therapy treatment for alcohol misuse. Exclusion criteria were: diagnosis of a co-morbid major psychiatric disorder (e.g., Schizophrenia or Bipolar Disorder), organic brain syndrome, alcohol related medical complications or heavy sedation. Participants were detoxified prior to assessment and completed the Toronto Alexithymia Scale (TAS-20) and the Revised Adult Attachment Scale (RAAS) as part of a larger study.

**Results:** TAS-20 total score, difficulties identifying feelings, difficulties describing feeling and externally oriented thinking were significantly positively associated with anxious attachment,  $r = .49$ ,  $p < .0001$ ;  $r = .53$ ,  $p < .0001$ ;  $r = .36$ ,  $p < .0001$ ;  $r = .25$ ,  $p < .01$ , respectively, but were not significantly associated with close or dependent attachment. Further, MANOVA indicated that alexithymic alcoholics reported significantly higher levels of anxious attachment and significantly lower levels of closeness (secure attachment) compared to non-alexithymic alcoholics, Wilks' Lambda  $F(6, 276) = 5.76$ ,  $p = .0001$ , power = .99 (comparisons significant by Tukey HSD post-test).

**Conclusions:** These findings support attachment theory indicating a positive relationship between anxious attachment and alexithymia, as well as significantly higher levels of insecure attachment in those with combined alexithymia and alcohol misuse compared to those with alcohol misuse alone.

**Support:** Institute of Health and Biomedical Innovation, Queensland University of Technology research scholarship.

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**BACK OUT THERE: SUBJECT RETRIEVAL AMONG RECOVERING POPULATIONS.**

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**Aims:** Research has documented inherent difficulties in tracking respondents of various "hidden populations" that often express a vested interest in remaining hidden, posing serious recruitment challenges to drug researchers. This presentation examines various tools successful for locating and accessing members of one hidden population, long-term recovering poly-substance abusers, many former intravenous drug users.

**Methods:** Twenty-five former heroin, cocaine, and other drug using respondents (ten female and fifteen male) were recruited and interviewed qualitatively. The similarities and differences between their strategies for maintaining abstinence from heroin and polydrug use are analyzed by gender and facilitated recruitment efforts. Eligibility included sustained abstinence from heroin for a period greater than five years, after a career of using heroin on an almost daily basis for a year or more.

**Results:** More than seventy persons were contacted initially or responded to recruitment flyers. More than half of those contacted were ineligible to participate in the research study for reasons described. For the women in the study, their abstinence efforts included the influence of familial and interpersonal relationships, as well as specific tools such as meditation and exercise. Men reported stable & lasting relationships. Both mentioned awareness of honesty with self and others, a sense of faith and spirituality, responsibility for behaviors and actions, and engaging others in their abstinence efforts.

**Conclusions:** Among the various experiences and successes experienced by these former heroin users, one of the most salient was peer support for maintaining abstinence from hard drug use. Understanding that they are responsible for others as well as themselves proved instrumental in their maintaining abstinence as well as assisting in recruitment efforts. Despite being a hidden population, many (women especially) wanted to tell their stories and describe the ongoing process of their long-term recovery. Additional research should investigate the multifaceted utility of peer support and gender differences in the process of long term recovery.

**Support:** NIDA R01 DA021783-04

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**RESULTS FROM A ONE-SESSION HIV RISK REDUCTION INTERVENTION IN ADOLESCENTS WITH SUBSTANCE USE DISORDER.**

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**Aims:** Young people with psychiatric and substance use disorders are at highest risk for contracting HIV. However, there are few data assessing HIV risk reduction interventions for this population. Addressing this research gap, this study aims to assess the impact of a one-session HIV risk reduction intervention acutely and at 12-month follow-up.

**Methods:** The research participants were a subsample of a larger 16-week trial of fluoxetine + CBT versus placebo + CBT for depression in adolescents, 13-19 years, with substance use disorder (SUD) and conduct disorder. The subsample of 50 received 16 weekly sessions of outpatient CBT for SUD that included one session of HIV risk reduction that focused on improving information and enhancing condom use. The main outcome measure was the Teen Health Survey (THS) administered before and after the intervention and at 3-, 6-, 9-, and 12-month follow-up. The Timeline Followback interview was used to assess specific sexual behaviors at 3-, 6-, 9-, and 12-month follow-up.

**Results:** There was a significant pre/post improvement of 2.7 points in the THS information subscale scale that was sustained at 12-month follow-up. There was a significant pre/post improvement in the THS Beliefs About Condom Use subscale of 0.9 points that was not sustained at 12-month follow-up. No other subscale showed a significant pre/post change.

**Conclusions:** These data support the feasibility of a one-session intervention for HIV risk in youth with SUD. However, more research is needed to determine the optimal dose and focus of the intervention.

**Support:** Supported by AACAP/NIDA 5K12DA000357

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**ECOLOGICAL MOMENTARY ASSESSMENT OF SMOKING CESSATION IN SMOKERS WITH SCHIZOPHRENIA.**

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**Aims:** There is a high prevalence ( $\geq 70\%$ ) of smoking among people with schizophrenia. These smokers have very low cessation rates, even when motivated to quit. In this pilot study, we used Ecological Momentary Assessment (EMA) techniques to study factors associated with smoking lapses in smokers with schizophrenia who were undergoing an unaided quit attempt.

**Methods:** Participants used hand-held computers to report their smoking behavior, mood, and exposure to smoking cues for 7 days before and 14 days after a self-initiated quit attempt. Participants were asked to (1) enter every cigarette smoked and complete reports on a random sample of these events; (2) complete 4-5 non-smoking reports per day when audibly prompted; (3) complete an "I've Quit" entry when they initiated a quit attempt; and (4) provide a breath CO sample 5 h later to corroborate self-report.

**Results:** Nine participants (66% male,  $45.7 \pm 8.6$  years old,  $27.3 \pm 5.5$  CPD) enrolled and 7 completed the 21-day study. The 8 participants who completed at least one week of monitoring completed 79.5% of 609 possible random prompt interviews, indicating acceptable EMA compliance. Seven out of 8 participants (88%) initiated a quit attempt and provided breath CO samples 5 h later that were consistent with quitting. Five participants lapsed within 2 days and all but one relapsed within 14 days of the quit attempt. Planned analyses will examine lapse precipitants (craving, mood, smoking cues) by comparing data collected at the first lapse to those collected in a non-smoking assessment completed within 1 hr of quitting.

**Conclusions:** Most study participants were compliant with EMA for 21 days and made a biochemically-verified quit attempt. These data support the feasibility and potential utility of using EMA to understand smoking relapse risk factors in this population.

**Support:** Supported by a Research Excellence Award to JWT from Brown University's Center for Alcohol and Addiction Studies.

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**PREDICTORS OF CUE-INDUCED CRAVING FOR METHAMPHETAMINE IN SUBJECTS WITH RECENT METHAMPHETAMINE ABUSE OR DEPENDENCE.**

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**Aims:** Methamphetamine (METH) dependence continues to be an important public health problem in much of the United States. Craving for METH is commonly reported by heavy users of the drug and may contribute to the progression of dependence as well as the risk of relapse in newly abstinent individuals. As for other drugs of abuse, craving for METH may be reliably measured in the laboratory but is not universally observed in all persons with METH abuse or dependence. The present study evaluated a number of demographic and clinical characteristics as predictors of craving upon exposure to METH-associated cues in 40 subjects meeting criteria for abuse or dependence within the past six months.

**Methods:** Subjects with urine screens negative for METH were presented with a sequence of simulated drug paraphernalia, 35-40 still photos, or 8-12 minutes of video depicting METH use in a balanced order. Subjective and physiological (heart rate, skin conductance) reactivity was measured prior to (baseline) and 60 seconds after cue presentation.

**Results:** Craving was reported by 47.5% of subjects at baseline and by 77.5% of subjects after cue exposure. Baseline craving was strongly predictive of cue-induced craving ( $p < .001$ ). No differences in craving were associated with age, sex, education, employment, or marital status. Subjects with abstinence in the past 30 or 60 days reported significantly less baseline ( $p < .05$ ) and cue-induced ( $p < .01$ ) craving than those with ongoing METH use. Cue-induced craving was significantly correlated with number of using days ( $p < .005$ ), total dollar amount used ( $p < .005$ ), and amount used per using day ( $p < .005$ ) in the 60 days prior to testing. A trend toward association of craving with the number of days since last use ( $p < .06$ ) was evident. Craving was not associated with amount of METH used at last using day ( $p < .34$ , NS).

**Conclusions:** The present results indicate that in this sample, craving for METH is reported by a majority of participants and is significantly associated with extent and recency of METH use.

**Support:** Supported by NIDA grant P20 DA022658 - See (PI), Brady (Co-I)

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**SUPPRESSION OF DOPAMINE-RELATED SIDE EFFECTS OF MORPHINE BY ATYPICAL ANTIPSYCHOTIC DRUGS INCLUDING A DOPAMINE SYSTEM STABILIZER.**Kazuhiro Torigoe<sup>1</sup>, M Narita<sup>1</sup>, D Takei<sup>1</sup>, M Shiokawa<sup>1,2</sup>, Y Matsushima<sup>1</sup>, S Takagi<sup>1</sup>, M Narita<sup>1</sup>, T Suzuki<sup>1</sup>, T Amano<sup>1,3</sup>, N Kuzumaki<sup>1</sup>, T Suzuki<sup>1</sup>; <sup>1</sup>Toxicology, Hoshi Univ. Sch. Pharm. Pharmaceut. Sci., Tokyo, Japan, <sup>2</sup>Pharmacy, St. Luke's International Hospital, Tokyo, Japan, <sup>3</sup>Molecular and Pharmacological Neuroscience, Division of Integrated Medical Science, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan

**Aims:** Dopamine receptor antagonists are commonly used to counter the adverse effects of opioids such as confusion, hallucinations, delusions and emesis. However, most of these agents themselves have side effects, including extrapyramidal symptoms. Here we investigated the effect of atypical antipsychotic drugs on morphine-induced dopamine-related actions in animals.

**Methods:** Evaluation of emetic response. Conditioned place preference test. Catalepsy scoring. ELISA. Rat in vivo microdialysis study and quantification of dopamine.

**Results:** The emetic effect of morphine was significantly suppressed by pretreatment with prochlorperazine (0.3 mg/kg, s.c.), perospirone (0.1 mg/kg, s.c.) or aripiprazole (10 mg/kg, s.c.) in ferrets ( $p < .05$ ). The morphine-induced place preference was significantly suppressed by prochlorperazine (0.3 mg/kg, s.c.), perospirone (0.3 mg/kg, s.c.), blonanserin (0.3 mg/kg, s.c.) or aripiprazole (20 mg/kg, s.c.) in mice ( $p < .05$ ). Catalepsy and the serum levels of prolactin were not observed by treatment with aripiprazole (40 mg/kg, s.c.) in mice, whereas other atypical antipsychotic drugs at relatively high doses showed both actions. The dopamine release in the nucleus accumbens stimulated by morphine (10 mg/kg, i.p.) was significantly decreased by pretreatment with aripiprazole (20 mg/kg, i.p.) in rats ( $p < .05$ ), whereas the morphine-induced dopamine elevation was enhanced by prochlorperazine (0.3 mg/kg, i.p.) ( $p < .01$ ).

**Conclusions:** These results suggest that aripiprazole may be more useful for reducing the severity of morphine-induced dopamine-related side effects rather than any other antipsychotics.

**Support:** Grants from the Ministry of Education, Culture, Sports, Science and Technology of Japan (Frontier Research).

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**VALIDATION OF THE CLINICAL OPIATE WITHDRAWAL SCALE.**David A Tompkins<sup>1</sup>, J A Harrison<sup>1</sup>, G E Bigelow<sup>1</sup>, R E Johnson<sup>2</sup>, P J Fudala<sup>2</sup>, L J Felch<sup>1</sup>, E C Strain<sup>1</sup>; <sup>1</sup>Psychiatry, The Johns Hopkins University School of Medicine, Baltimore, MD, <sup>2</sup>Reckitt Benckiser Pharmaceuticals Inc., Richmond, VA

**Aims:** The COWS is an 11-item clinician administered scale to assess opioid withdrawal. Total scores can range from 0 to 48 and classify withdrawal as mild, moderate, moderately severe or severe. Though commonly used in clinical practice, this scale has never been validated. The present study validated the COWS against the validated Clinical Institute Narcotic Assessment (CINA) scale in an opioid-dependent population undergoing a naloxone (N) challenge.

**Methods:** Out-of-treatment opioid-dependent subjects participated. After morphine stabilization on 30 mg SQ 4x daily, subjects underwent a double blind randomized challenge of IM placebo (P) or N (0.4 mg) on separate days. During challenges, COWS, CINA scales, and visual analog scales (VAS) were concurrently obtained. Those persons who successfully differentiated between N and P were included in the present analysis. Correlation analyses were calculated on peak COWS and CINA scores as well as VAS self-report items of drug effect. Cronbach's alpha was used to determine the internal consistency of individual items on the COWS.

**Results:** Subjects ( $n=38$ ) were primarily male (68%), Caucasian (66%) and had a mean age of 40.8 years. Mean peak COWS score of 15.1 occurred on average 30 minutes post-injection of N at which time the mean CINA score was 24.2. Mean COWS and CINA scores 30 minutes after placebo injection were 0.52 and 18.3, respectively. Pearson correlation coefficient for mean peak COWS and CINA scores was 0.82 ( $p < .0001$ ) during the N challenge session. Mean COWS scores also correlated well with mean VAS scores of bad drug effect ( $r=0.503$ ) and feeling sick ( $r=0.534$ ). P produced no significant elevation of COWS or CINA scores throughout the 150-minute study session. Cronbach's alpha score was 0.77, indicating good internal consistency.

**Conclusions:** COWS is a valid measurement tool for acute opiate withdrawal in dependent individuals.

**Support:** This project was supported by a contract from Reckitt Benckiser Pharmaceuticals Inc. as well as NIDA grants DA08045, DA023186, and T32DA07209.

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**EXAMINING THE RELATIONSHIP BETWEEN RISK OF CRIMINAL RECIDIVISM AND SUBSTANCE USE AND TREATMENT HISTORY IN A SAMPLE OF PROBATIONERS.**A J Trotman<sup>1</sup>, M E Wilson<sup>2</sup>, F S Taxman<sup>1</sup>; <sup>1</sup>Administration of Justice, George Mason University, Manassas, VA, <sup>2</sup>Friends Research Institute, Baltimore, MD

**Aims:** An important factor in determining how to best provide treatment for criminally involved substance dependent individuals is identifying variables that impact treatment outcome. The aim of the current study is to determine whether risk for criminal recidivism is related to frequency or severity of drug use or treatment history. We hypothesize high risk subjects will exhibit greater drug use and treatment history.

**Methods:** A randomized trial is being conducted to examine the impact of integrated substance abuse treatment and community supervision on several outcome variables. Empirically supported manualized treatment is provided on-site at three probation offices in Maryland and compared to treatment in the community. Follow-up data is collected at 3-, 6-, and 12-months post-randomization. Subjects are blocked on level of recidivism risk at baseline. Subjects are classified as low-moderate risk (LR) or high risk (HR) as determined by several criminal history variables (e.g., total number of lifetime arrests). Baseline data for 173 subjects are presented (LR = 108, HR = 65).

**Results:** Chi-square analyses show differential effects by recidivism risk on percentage of subjects positive for drug use (LR = 36.4%, HR = 55.4%;  $\chi^2 = 5.90$ ;  $p < .01$ ). One-way ANOVAs show significantly higher mean number of different drug positives at baseline for HR ( $M = 0.77$ ,  $SD = 0.86$ ) compared to LR ( $M = 0.45$ ,  $SD = 0.66$ ;  $p < .01$ ), and significantly higher self-reported number of times subjects have ever received substance use treatment for HR ( $M = 2.45$ ,  $SD = 3.29$ ) compared to LR ( $M = 1.50$ ,  $SD = 2.07$ ;  $p < .05$ ) as well.

**Conclusions:** These results suggest that risk of recidivism is related to variables that impact substance abuse treatment outcome. These results, coupled with previous research demonstrating the relationship between recidivism risk and treatment outcome, underscore the importance of considering recidivism risk when assessing individuals to determine the most appropriate treatment.

**Support:** Supported by NIDA R01 DA017729; F. S. Taxman, PI.

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# VALIDATION OF COMPREHENSIVE HEALTH ASSESSMENT TOOL: AN INTERACTIVE, MULTIMEDIA SCALE TO ASSESS ALCOHOL AND SUBSTANCE ADDICTION SEVERITY AMONG ADOLESCENTS.

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**Aims:** To construct a valid and reliable interactive, multimedia, self-report scale on alcohol and substance addiction severity among adolescents for use in treatment settings.

**Methods:** A total of 356 adolescents (ages 13 – 18) participated in this study. The normative sample included 94 adolescents from two high schools in Massachusetts. The treatment sample included two groups: Test-retest was conducted with 49 adolescents. Comparison measures and the scale were completed by another 213 adolescents.

**Results:** Results from a confirmatory factor analysis (using maximum likelihood estimation) revealed a valid model measuring addiction severity, (39) = 61.57,  $p=.01$ , CFI = .99, RMSEA = .04. The model consists of six domains: (1) Family Relations, (2) Peer Relations, (3) Psychological Issues, (4) Tobacco Use, (5) Alcohol Use, and (6) Substance Use. Each domain has two manifest variables, one variable measuring severity (e.g., number of psychological symptoms) and the other variable measuring frequency of problem (e.g., number of days in the past 30 days had psychological problems). All manifest variables measure current or recent (past 30 days) level of functioning. Domain level test-retest reliability ranged from  $r = 0.62$  to as high as  $r = 0.91$ . Convergent/Discriminant validity was measured by examining bivariate correlations between each domain and comparison measures. As expected, comparison measures were more highly correlated with the target domain as compared to other domains. Domain level composite scoring was derived from the normative sample of 94 participants from local high schools.

**Conclusions:** The Comprehensive Health Assessment Tool (CHAT) has acceptable validity and reliability for use in the treatment setting.

**Support:** This study was supported by an SBIR grant awarded to Inflexxion (NIDA: 5R44D A014139-04, PI: Sarah Lord).

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# THE EFFECT OF TEACHER-RATED ATTENTION-CONCENTRATION PROBLEMS IN GRADES 1 THROUGH 6 ON LATENT CLASS GROWTH TRAJECTORIES OF HALLUCINOGENS, ECSTASY/MDMA, KETAMINE, SEDATIVES, AMPHETAMINES/STIMULANTS, ANALGESICS, TRANQUILIZERS, INHALANTS, COCAINE, AND HEROIN FOR FEMALES AGED 19-20.

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**Aims:** This study sought to identify early childhood predictors of later drug use for females.

**Methods:** Teacher ratings of attention/concentration problems were obtained in Grades 1-6 in a sample ( $n=663$ ) of females. Drug use data was obtained at age 19-20.

**Results:** Using GMMs, we found two classes that are significantly different for hallucinogens use (Chi-square=5.804,  $p=.03$ ), ecstasy (Chi-square=3.711,  $p=.05$ ), and Ketamine use (Chi-square=3.653,  $p=.05$ ). We found two classes that are significantly different for frequency sedatives were taken for non-medical reasons (Chi-square=6.588,  $p=.01$ ), last time a sedative had been taken for non-medical reasons (4.795,  $p=.01$ ), and frequency sedatives were taken for non-medical reasons during the past twelve months (6.356,  $p=.01$ ). We found two classes that were significantly different for the frequency amphetamines/other stimulants were taken for non-medical reasons (Chi-square=4.714,  $p=.03$ ), use of analgesics without a prescription (Chi-square=4.305,  $p=.04$ ), and frequency tranquilizers were taken for non-medical reasons (Chi-square=3.691,  $p=.05$ ). We also found two classes that were significantly different for age when first used inhalants (Chi-square=3.660,  $p=.05$ ) and frequency of inhalants use in the past twelve months (Chi-square=7.062,  $p=.008$ ). We also found two classes that were significantly different for frequency of cocaine use in the past twelve months (Chi-square=4.346,  $p=.04$ ), frequency of cocaine use in the past month (Chi-square=22.743,  $p=.0000$ ) and last time of cocaine use (Chi-square=7.025,  $p=.008$ ). We found two classes that were significantly different for frequency of heroin use for the past twelve months (Chi-square=6.117,  $p=.01$ ).

**Conclusions:** Findings highlight critical need for addressing attention/concentration problems early in life.

**Support:** Study supported by T 32 grant.

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# RE-ENTRY STRATEGIES FOR CALIFORNIA EX-OFFENDERS.

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**Aims:** The Alameda County Public Health Department commissioned Regional Congregations and Neighborhood Organizations Training Center to survey African American faith-based organizations in East Oakland, West Oakland and Hayward to provide the county with baseline information on faith and community efforts to reintegrate residents returning from prison. The survey will inform public health strategies.

**Methods:** Fifty faith- and community-based organizations participated in a convenience survey to determine how best to provide medical services to the reentry community of Alameda County that is non-fragmented, reduces waiting periods and provide quality health care especially for chronic health issues like substance abuse, HIV, diabetes, hypertension and heart disease.

**Results:** The Results indicated that: 27% of churches have 396 transitional beds for substance abuse treatment and mental health treatment; 90% of churches of the churches already have 501(c)3 status with tax-exempt status under Sec 501(c)(3) of the Internal Revenue Code demonstrating readiness to receive funding from governmental and private sources; 44% had budgets of \$100,000 to \$500,000; workforce staff is 88% volunteer; 42% have the membership have a range of training in administrative office areas, human resources; top issues of concern for congregations were: substance abuse (25%); housing (23%); education (21%); and crime (17%); 29% have membership between 100-199 members, 13% between 200-299 members, 10% between 600-699; 10% between 0-99 members, 8% between 300-399 members, 8% between 400-499 members, and 6% with 1,000 members and above; major obstacles in churches achieving their goals are lack of funding and resources 48%, lack of paid staff 33%, lack of adequate facilities (21%) and leadership to accomplish goals (21%).

**Conclusions:** It is clear that churches in the Bay Area can be an untapped source for re-entry efforts in collaboration with Alameda County. However, it is also clear that there are internal and external issues that need to be addressed in order to ensure these churches are viable.

**Support:** The California Endowment: Grant #20062072

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# GENDER DIFFERENCES IN PSYCHOSOCIAL STRESS AND IN ITS RELATIONSHIP TO GAMBLING URGES IN INDIVIDUALS WITH PATHOLOGICAL GAMBLING.

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**Aims:** Pathological gambling (PG) bears striking parallels to drug addiction. For instance, heightened levels of stress and arousal have been implicated in the course of both, PG and addictive disorders. Even though epidemiological surveys consistently demonstrate gender-related differences in the prevalence of PG (men>women), similar differences in the amount of stress and their relationship to gambling activities have not yet been investigated. The purpose of this pilot study was to evaluate potential gender differences in psychosocial stress exposure among non-treatment seekers with PG and to relate such differences to the measures of gambling.

**Methods:** The study participants included 14 male and 9 female individuals matched by demographic characteristics and severity of PG. We used the Daily Stress Inventory (DSI) along with multidimensional questionnaire that assesses various aspects of gambling urges including: (a) current intensity, (b) projected intensity, (c) resistance to gambling, (d) responsiveness to gambling-related conditioned stimuli, and (e) imagined likelihood of gambling if in a setting with access to it.

**Results:** Females displayed higher ( $t=2.1$ ;  $df=21$ ;  $p=0.05$ ) Impact Scores ( $145.7 \pm 47.9$  vs.  $84.0 \pm 90.5$ ) on the DSI than male subjects. Another measure of stress, obtained with the Profile of Mood States, was also significantly elevated in the PG females ( $p<0.05$ ). Furthermore, DSI stress levels significantly correlated with self-reported gambling urges in the male ( $r=0.8$ ;  $df=12$ ;  $p<0.001$ ) but not in the female subjects.

**Conclusions:** These data suggest distinctive features of psychosocial stress effects in women with PG vis-à-vis those of men. A possible explanation for these findings may involve modulatory effects of estrogen on stress- and motivation-related dopaminergic systems. Further studies will be needed to confirm these observed gender differences and to investigate their possible mechanisms, particularly estrogen-dopamine interactions and their effect on gambling urges and activities.

**Support:** This work was supported by grant DA # 017959 (IE) from the National Institute on Drug Abuse.

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**MATHEMATICAL MODEL OF EFFECTS OF FIRST ORDER SCHEDULES ON DRUG SELF-ADMINISTRATION.**

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**Aims:** Schedules of reinforcement are widely used as an important tool to study the reinforcing properties of drugs and natural reinforcers. Comprehensive mathematical models of ratio and interval schedules of drug delivery illustrated by cocaine self-administration data will be presented.

**Conclusions:** A schedule of reinforcement is the protocol determining conditions under which responses or behaviors will result in the delivery of a reinforcer. Schedules may be viewed as limitations on the availability of a reinforcer, requiring a certain number of responses to be performed (ratio schedules) or a certain period of time to elapse between reinforcer deliveries (interval schedules). Ratio/interval schedules can be fixed or variable and the latter can be divided into several subgroups (progressive, random etc.). According to our pharmacological theory of drug self-administration, after the acquisition of drug self-administration behavior under first order schedules, drugs have two effects – response-induction and response-inhibition. Which of these two opposite effects will occur at a particular time depends on the concentration of the drug at the site of action. The drug of abuse will induce responding in trained animals only when its concentration is within the compulsion zone, i.e., above the priming/compulsion threshold and below the satiety threshold. This drug will not induce responses when its concentration is too low, i.e., below the compulsion/remission threshold. The drug will selectively inhibit the same response when its concentration is above the satiety threshold. Schedules of drug delivery other than Fixed Ratio = 1 and Fixed Interval = drug delivery duration result in an increased time during which drug concentrations are within the compulsion zone. Consequently, schedules influence the drug consumption rate. Both the drug consumption and drug elimination rates define drug concentration and, therefore, periods of time when a drug induces or inhibits responding. Cocaine and food self-administration behavior under the fixed ratio schedule will be compared.

**Support:** NIDA grants DA14189 and DA018538

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**MOTIVATORS OF CHANGE AMONG DRUG USING NEW ORLEANS EVACUEES.**R Twigg<sup>2</sup>, N Tiburcio<sup>1</sup>, Bruce D Johnson<sup>1</sup>, E Dunlap<sup>1</sup>; <sup>1</sup>Special Populations Research, National Development and Research Institutes, New York, NY, <sup>2</sup>Social Work, Fordham University, New York, NY

**Aims:** The Katrina disaster in August 2005 disrupted lives, forced relocation and resulted in monumental costs and emotional turmoil. The total flooding of low lying areas in New Orleans, forced many residents to relocate to host cities (for example Houston, Baton Rouge and Memphis). The study presented here was uniquely situated in that it recorded individual changes in drug use patterns during various timepoints relative to the disaster. In order to provide an in-depth understanding of the disruption, adaptation and reemergence of drug use patterns and markets pursuant to the disaster and relocations, we examine (1) Changes experienced by these individuals at the personal and environmental levels and (2) Re-occurring themes in how these changes impacted motivation to reduce substance use.

**Methods:** Based on transcript material from qualitative interviews with 107 New Orleans Evacuees selected in New Orleans and Houston in 2006 and 2007, this presentation describes the population, their drug use patterns prior to the Katrina disaster, during evacuation, once settled in to their host communities, and analyzes how the relocation efforts affected their drug use and drug dealing markets.

**Results:** Evacuees reported experiencing multilevel changes (micro, mezzo, and macro). A review of the recurring themes reveals that an important minority reported enhanced motivation to reduce their substance use patterns at time of interview. In contrast, others successfully located their previous drugs of choice or substituted drugs within these new host communities.

**Conclusions:** Amidst the traumatic experiences shared by Katrina evacuees, some substance-using individuals reported increased motivation to reduce or discontinue their substance use. This suggests that additional disaster research should investigate changes in individual drug use patterns pursuant to disasters. In the future, more rapid public health efforts can be tailored to maximize such motivation.

**Support:** Disruption and reformulation of illegal drug markets among New Orleans Evacuees(NIDA: R01 DA021783-04).

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**DELIVERY AND NEONATAL OUTCOMES OF METHADONE MAINTAINED PREGNANT PATIENTS WITH AND WITHOUT A CURRENT MOOD DISORDER.**Michelle Tuten<sup>1</sup>, H Jones<sup>1</sup>, K O'Grady<sup>2</sup>, H Fitzsimons<sup>1</sup>, S Heil<sup>3</sup>, M Chisolm<sup>1</sup>; <sup>1</sup>Johns Hopkins University, Baltimore, MD, <sup>2</sup>University of Maryland, College Park, College Park, MD, <sup>3</sup>University of Vermont, Burlington, VT

**Aims:** The study examined two primary questions: (1) Do women with a current mood disorder have poorer maternal delivery outcomes compared to women without a current mood disorder? (2) Do women with a current mood disorder have poorer neonatal outcomes compared to women without a current mood disorder?

**Methods:** Participants ( $N=68$ ) were enrolled in a comprehensive drug treatment program, completed the SCID-I interview for DSM-IV diagnoses and met criteria for current opioid dependence. Participants were categorized into two groups based upon current mood disorder diagnosis: (1) absence of mood/anxiety disorder ( $n=30$ ), or (2) primary mood disorder ( $n=38$ ). Maternal and neonatal delivery data were abstracted from patient records.

**Results:** The sample had a mean age of 30 years ( $SD=5.9$ ), 10.8 years of education ( $SD=1.7$ ), were predominately Black (74%) and unemployed (93%). The primary drugs used prior to intake were: heroin (93%), cocaine (76%), alcohol (22%) and nicotine (97%). Delivery outcomes were similar between groups. Overall, 82% delivered vaginally and the mean length of maternal hospital stay was 2.8 days ( $SD=1.1$ ) following delivery. Neonatal outcomes differed between groups with infants of mood disordered women remaining in the neonatal intensive care unit (NICU) 6 times longer than infants of control women (3.1 ( $SD=1.6$ ) versus .5 days ( $SD=.4$ ), respectively ( $p=.05$ ). Although not reaching conventional statistical significance, infants of mood disordered women tended to be born earlier in gestation ( $p=.16$ ), be premature ( $p=.11$ ) and to be admitted to the NICU ( $p=.12$ ) compared to infants of women without a mood disorder.

**Conclusions:** These findings document the negative impact that current mood disorders can have on the neonate. Assessment and treatment of co-occurring mood disorders is an important component of comprehensive care for methadone maintained pregnant patients.

**Support:** NIDA R01 DA12403

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**PREDICTORS OF ALCOHOL- AND/OR DRUG-RELATED CONSENSUAL AND UNWANTED SEXUAL ENCOUNTERS.**

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**Aims:** To examine predictors among college students of alcohol- and/or drug-related consensual and unwanted sexual encounters.

**Methods:** The Core Alcohol and Drug Survey, which examines alcohol- and drug-related behavior within the past year, was administered to students at a mid-sized suburban university ( $n=565$ , 65% female). Outcomes were assessed in terms of: whether the last sexual encounter involved alcohol (yes *v* no) or other drugs (yes *v* no) and whether the student reported having been taken advantage of sexually as a result of drinking or drug use (yes *v* no). Predictor variables included: age, gender, ethnicity (white *v* non-white), alcohol consumption (yes *v* no) and illicit drug use (yes *v* no) in the past 30 days; the belief that alcohol facilitates sexual opportunities (yes *v* no); and average number of drinks consumed in the past 30 days.

**Results:** Results revealed that as age increased, the likelihood decreased that the last sexual encounter involved alcohol (Odds Ratio [OR] = 0.84,  $p=.05$ ), the last sexual encounter involved other drugs (OR = .70;  $p=.04$ ), or that the individual had been taken advantage of sexually while under the influence of alcohol or drugs (OR = .8,  $p=.04$ ). Conversely, the likelihood that the last sexual encounter involved alcohol (OR = 1.4,  $p=.02$ ) increased with the average amount of alcohol consumed per week. Females were significantly less likely than males to report that their last sexual encounter involved illicit drugs (OR = .17;  $p<.001$ ). Finally, the likelihood of having been taken advantage of sexually while under the influence of alcohol or drugs was greater when students reported having consumed alcohol in the past 30 days (OR = 4.2;  $p=.06$ ) or expressed the belief that alcohol facilitates sexual opportunities (OR = 2.6;  $p=.02$ ).

**Conclusions:** Older age may be a protective factor with regard to alcohol- and drug-related sexual encounters. Students who believe that alcohol facilitates sexual opportunities may place themselves in drinking situations that increase their risk of being taken advantage of sexually.

**Support:** This research was supported by a grant from the Maryland Alcohol and Drug Abuse Administration.

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**TRAUMA EXPOSURE, DISTRESS AND SELF-REPORTED DRUG USE.**

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**Aims:** Post Traumatic Stress Disorder (PTSD) may correlate with psychological distress and drug use severity. The study evaluates life-time trauma exposure, PTSD symptoms, psychological distress and self-reported drug use among admissions to a study of cocaine dependence treatment during methadone maintenance.

**Methods:** Data were collected from 80 subjects (AA: 41, F: 38, age  $42 \pm 6.9$  years) enrolled in an ongoing clinical trial of topiramate for cocaine dependence during the 5-week pre-randomization. Measures included Traumatic Life Event Questionnaire [TLEQ], PTSD symptom Scale (PSS), Beck Depression Inventory [BDI], State-Trait Anxiety Inventory [STAI], Cocaine Selective Severity Assessment [CSSA], weekly self-reported IV and non-IV drug and alcohol use.

**Results:** On TLEQ, 75 subjects reported (mean  $\pm$  SD)  $15.3 \pm 9.7$  traumatic events, 5 denied any exposure. Median PSS score was 0, mean PSS total score was  $7.4 \pm 12.7$ . Women scored higher than men:  $11.7 \pm 15.7$  vs  $3.5 \pm 7.5$ . No differences in PSS scores were based on race or age. Overall, higher number of PSS symptoms seemed to predict higher STAI, CSSA and higher use of illegal methadone, cocaine, opiate and benzodiazepines, and less use of alcohol and marijuana on admission, but the difference disappeared at week 5. Only 4 women met criteria for PTSD based on PSS. PTSD subjects tended to score higher on the STAI-state ( $53.8 \pm 9.9$  vs  $44 \pm 10.3$ ,  $p=.07$ ), STAI-trait ( $52.3 \pm 6$  vs  $45 \pm 8.2$ ,  $p=.09$ ), and CSSA ( $72.8 \pm 9.4$  vs  $52.3 \pm 18.9$ ,  $p=0.04$ ) on admission. The differences remained borderline significant at week 5 for the STAI-state ( $47.5 \pm 11.7$  vs  $39.4 \pm 8.9$ ,  $p=.08$ ), but not for other measures.

**Conclusions:** preliminary results showed high trauma exposure but low symptom severity among cocaine and opiate dependent participants (with no benzodiazepine dependence). Higher PSS scores tended to predict higher anxiety and cocaine craving, and more drug use on admission. Some of these differences disappeared during the first treatment weeks.

**Support:** NIDA grants: DA021808, T32DA07209

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**IRISH TRAVELLERS AND DRUG USE.**

Marie Claire A Van Hout; Health, Waterford, Waterford, Ireland

**Aims:** The Traveller Community are identified "as people with a shared history, culture and traditions including, historically, a nomadic way of life on the island of Ireland". This ethnic minority present with lower but similar levels and patterns of drug use than the general population, but are particularly vulnerable to early onset of drug use and problematic substance use relating to poor mental health, low literacy levels, unemployment and discrimination within their communities. The research aimed to explore the recent issue of drug use in the Traveller community and research findings were used to guide resources for those Travellers at risk of early onset of drug use and those experiencing drug related difficulties.

**Methods:** The research consisted of a random sample of 12 focus groups of Travellers ( $n=57$ ) with a gender balance (47/53%) in halting sites across the Western Region of Ireland. A themes analysis was conducted and grounded in the information garnered.

**Results:** The Travellers indicated a fear of fragmentation of their culture and reported increased awareness of drug use and drug dealing within their communities. Problematic drug use was common among Traveller men and exacerbated by unemployment, depression, and increasing contact with the settled community. In contrast Traveller women had little contact with illicit drugs and reported increasing problematic use of prescription medication. There is a stigma attached to drug addiction within the Traveller communities with families often attempting home detoxification without outside support. The Travellers were especially concerned about heightened levels of domestic abuse, difficulties in engaging in residential treatment, comprehension of harm reduction information and the lack of culturally appropriate drug addiction services.

**Conclusions:** In order to fully respond to the issue of increasing drug use among the Traveller community, targeted and culturally appropriate drug service provision must be developed in order to integrate Travellers and settled individuals in outreach, education and treatment.

**Support:** This research was funded by the Western Regional Drugs Task Force, Ireland.

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**EVALUATION OF CRIMINAL JUSTICE DIVERSION: CALIFORNIA'S PROPOSITION 36.**

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**Aims:** To report show rates, completion rates, re-arrest rates and costs associated with California's Proposition 36. To discuss the impact of recent budget cuts and suggest strategies for potential improvement in implementation and legislation.

**Methods:** Secondary analyses of statewide administrative databases were performed to describe outcomes. Outcomes were examined by treatment status (not treated, treated but not completed, completed) within the Prop 36 era, and by comparing re-offending among Proposition 36 eligible offenders to similar offenders in the pre-Proposition 36-era.

**Results:** Each year, 70-75% of offenders referred to treatment have been admitted, and one third of those admitted complete treatment. Re-offending was lowest among Proposition 36 offenders who completed treatment compared to offenders who did not, but Proposition 36-era offenders had a higher rate of drug and property arrests than a pre-Proposition 36-era comparison group. Over a 42 month followup period, Proposition 36 saved taxpayers \$2 for every \$1 invested.

**Conclusions:** Proposition 36 successfully diverted thousands of offenders into treatment and saved taxpayer money, especially on incarceration. Show rates, completion rates, and arrest rates are not surprising, but there is room for improvement. Decreasing funding is a major barrier, but low-cost strategies such as process improvement (e.g. NIATx methods) and others are available and represent an important way forward during difficult financial times.

**Support:** California Department of Alcohol and Drug Programs

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**SEX EFFECTS ON NICOTINE WITHDRAWAL IN SMOKERS WITH AND WITHOUT ADHD.**

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**Aims:** Research in our laboratory and others' indicates that Attention-Deficit/Hyperactivity Disorder (ADHD) and increased levels of ADHD symptoms impact a range of smoking outcomes, but to date there is little information on how the effects differ in males and females. The purpose of this study was to explore sex differences during acute and prolonged smoking abstinence across 3 separate experiments of smokers with and without ADHD or high levels of ADHD symptoms.

**Methods:** Secondary data analyses from: 1) a completed laboratory study of the effects of acute overnight abstinence on smokers with ( $n=14$ ) and without ( $N=12$ ) ADHD; 2) an ongoing study of the effects of prolonged smoking abstinence (~2 weeks) in smokers with and without ADHD ( $N=31$  to date); and 3) two large-scale smoking cessation trials conducted through the Duke Center for Nicotine and Smoking Cessation Research ( $N=389$ ), in which self-reported baseline ADHD symptoms were collected.

**Results:** Female smokers with ADHD exhibited more pronounced withdrawal and worse success in smoking cessation when compared to female smokers without ADHD and to males with or without ADHD across a range of variables, including craving and negative affect. Female smokers with high levels of self-reported ADHD symptoms in smoking cessation trials lapsed significantly faster than females with low levels of ADHD symptoms or males with or without high levels of symptoms.

**Conclusions:** These findings suggest that the association between ADHD and smoking outcomes may be largely driven by female smokers. Additional work is needed to further characterize the moderating role of sex on the association between ADHD and smoking outcomes, as well as the mechanisms that underlie these findings.

**Support:** This work was supported by grants 1R21DA020806 (Kollins), 5K24DA023464 (Kollins) from the National Institute on Drug Abuse and an unrestricted grant from Philip Morris USA, Inc. (Rose)

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**PREDICTORS OF TREATMENT RETENTION IN A COMMUNITY SUBSTANCE ABUSE CLINIC.**Ryan Vandrey<sup>1</sup>, J Fry<sup>1</sup>, P Stabile<sup>2</sup>, M Stitzer<sup>1</sup>; <sup>1</sup>Johns Hopkins University, Baltimore, MD, <sup>2</sup>Harbel Treatment and Recovery Center, Baltimore, MD

**Aims:** Most who enter treatment for substance use problems have difficulty completing treatment. One approach to improving retention and outcomes is to identify modifiable characteristics of patients who complete treatment so that more intensive or specialized interventions can be given to those with a poor prognosis for retention. We sought to identify predictors of treatment retention at a community drug treatment clinic in Baltimore, Maryland.

**Methods:** A sample of 200 consecutively enrolled clients was selected, of which 184 attended at least one appointment following intake and were included in the study. Data was obtained for independent variables of age, sex, ethnicity, referral source, drug(s) used, poly drug use status, result of first urine drug screen, counselor assignment, and attendance at individual and group counseling sessions during the first 4 weeks of treatment. Retention for at least 90 days (dichotomous) was the dependent variable. A logistic regression analysis was conducted to identify independent variables that predicted 90-day retention.

**Results:** Result of the first drug test (positive for any drug or negative for all drugs) and number of individual and group counseling sessions attended during the first 4 weeks were significant predictors of treatment retention.

**Conclusions:** That those with an early negative urine drug screen predicted later treatment success replicates prior findings, but in a more diverse treatment sample. This suggests that drug testing early in treatment may be an effective strategy for identifying clients who require more intensive interventions to achieve positive outcomes. These findings also suggest that modification of clinic services to increase early treatment engagement is a potentially important strategy for improving client outcomes. Early engagement might be improved through diverse strategies such as shortening the time between intake and first counseling appointment, diligent use of appointment reminders, providing small incentives for attendance, or making counseling sessions more engaging for clients.

**Support:** NIDA/CTN U10 DA13034

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**INFLUENCE OF ACUTE METHYLPHENIDATE ADMINISTRATION ON CIGARETTE SMOKING BEHAVIOR IN ADHD DIAGNOSED ADULTS.**Andrea R Vansickel<sup>1</sup>, M Poole<sup>1</sup>, W W Stoops<sup>1</sup>, P E A Glaser<sup>2</sup>, C R Rush<sup>1,2</sup>; <sup>1</sup>Psychology, Behavioral Science, University of Kentucky, Lexington, KY, <sup>2</sup>Psychiatry, University of Kentucky, Lexington, KY

**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 the present investigation is to determine whether acute methylphenidate administration influences smoking behavior in ADHD diagnosed adults. We hypothesize that methylphenidate will increase smoking in ADHD diagnosed adults.

**Methods:** Eight to ten participants that smoke 10-20 cigarettes per day, currently meet diagnostic criteria for ADHD, are not prescribed ADHD medication and do not have other medical or psychiatric conditions (except nicotine dependence) will complete this study (3 have completed so far). Participants will complete six, 6-hour sessions (including one practice). Doses of methylphenidate (10, 20 and 40 mg) are tested once while placebo is tested twice. One hour after medication administration, participants are allowed to smoke ad libitum for four hours. Measures of smoking include total cigarettes smoked, total puffs, and carbon monoxide levels. Snacks and decaffeinated drinks are available ad libitum, and caloric intake during the four-hour smoking session is calculated. Data are analyzed statistically as raw scores using repeated measures ANOVA.

**Results:** Preliminary results indicate that acute administration of methylphenidate increases cigarette smoking and decreases caloric intake in ADHD diagnosed adults.

**Conclusions:** The results of this experiment extend previous findings regarding the effects of methylphenidate on smoking to a clinically relevant population. The current findings could have important clinical implications for the pharmacological management of ADHD in cigarette smokers or those that are at elevated risk to smoke.

**Support:** University of Kentucky, Pilot Grant Funds, Center on Drug and Alcohol Research, Department of Behavioral Science (Vansickel) University of Kentucky, Professorship Funds, Department of Psychiatry (Rush)

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**IMPULSIVITY, RISK-TAKING, AND BEHAVIORAL PROBLEMS IN TREATMENT-SEEKING ADOLESCENTS.**

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**Aims:** To examine the relationship between adolescent substance use, externalizing behaviors, and laboratory measures of impulsivity/decision-making and risk-taking.

**Methods:** Adolescents (n=70) and their parents completed an intake evaluation for substance abuse treatment. Youth reported recent substance use by the Timeline Followback Method (TLFB) and reported their age at first use. Adolescents were administered the Balloon Analogue Risk Task (BART) to evaluate risk-taking propensity and measures of delay discounting to assess impulsivity/decision-making. Parents reported on their children's externalizing behaviors on both the Antisocial Process Screening Device (APSD) and the Child Behavior Checklist (CBCL).

**Results:** No strong relationships were observed between participants' self-reported substance use (age of first use or days of use in last month) and laboratory measures of risk-taking or delay discounting. Adolescents discounted money and marijuana at equivalent rates for both the \$100 and \$1000 conditions. Externalizing symptoms, either alone or in combination with substance use variables, were not significantly related to either BART (adjusted average number of pumps) or delayed discounting (log k) assessments.

**Conclusions:** Current results contradict previous reports in adults of relationships between substance use variables, externalizing behaviors, and delayed discounting measures. Additionally, in this sample, marijuana and money were discounted at similar rates, which contrasts with adult data reflecting steeper discounting for drugs. This is a first step in observing risk-taking and decision-making in treatment-seeking adolescents and highlights the need for more information on developmental trends in both these areas, as well as exploration of the methodological differences that may influence these results. We will replicate these analyses with a larger sample size in the spring, as well as explore relationships with treatment outcome.

**Support:** NIDA: DA015186-06, NIAAA: AA016917, and the Arkansas Biosciences Institute-the major research component of the Tobacco Settlement Proceeds Act of 2000

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**INHALANT AND OTHER DRUG USE AMONG ROMA YOUTH IN CENTRAL AND EASTERN EUROPE: OUTLINE OF A RESEARCH PROGRAM.**Peter Vazan<sup>1</sup>, M Khan<sup>1</sup>, M Miovsky<sup>2</sup>; <sup>1</sup>Behavioral Sciences Training program, Public Health Solutions, New York, NY, <sup>2</sup>Center for Addictology, 1st Psychiatric Clinic of the Charles University Medical School, Prague, Czech Republic

**Aims:** The available, though rather sporadic, data on inhalant use among Roma population in Eastern Europe indicate widespread use primarily among children and adolescents who also initiate smoking and drinking at very early age. Because of the lack of systematic data, the aim of this paper is to describe a research program for collecting longitudinal data and monitoring drug use on an on-going basis. The development of a monitoring system will be the first stage in designing and implementing prevention programs tailored to the needs of Roma youth. The paper first reviews existing data on Roma substance abuse in order to understand the scope and nature of the problem. It is argued that extreme poverty and continued segregation and discrimination are the primary determinants of drug abuse in this population including alarming levels of use of volatile solvents such as toluene. Anecdotal reports documented that parents in some cases give toluene to children to suppress their hunger.

**Conclusions:** In 2005, the governments of nine countries (Bulgaria, Croatia, the Czech Republic, Hungary, Macedonia, Montenegro, Romania, Serbia and Slovakia) launched an unprecedented initiative to promote integration of Roma into the mainstream society. One of the priority areas of the *Decade of Roma Inclusion* is improvement of Roma health. To meet this goal, an effective monitoring mechanism is necessary in order to produce reliable data. Specifically, the infrastructure we propose for the data collection network will utilize standardized instruments tailored to Roma needs assessment, which will be administered by trained health mediators who have active and long-term presence in Roma settlements. The implementation of the proposed data collection infrastructure will enable both comprehensive between-country comparisons of Roma health indicators and also within-country comparisons with the majority population.

**Support:** Behavioral Sciences Training In Drug Abuse Research T32DA007233, Public Health Solutions

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**ATTITUDES TOWARD 12-STEP GROUPS AND REFERRAL PRACTICES IN A CULTURE NAIVE TO 12-STEP IDEOLOGY.**

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**Aims:** Addressing addiction effectively requires a long-term approach. Substance abuse treatment is typically limited in this respect. Participation in self-help groups is empirically associated with reductions in substance use and contributes to solidifying treatment gains. Thus referring clients to self-help groups such as 12-step groups (TSG) represents a promising complimentary resource. Studies of clinicians' attitudes toward and referral practices to the TSG have been conducted in countries where the 12-step philosophy is highly integrated with professional services. This study describes clinicians' attitudes about and referral practices to TSG in Norway where health authorities seek to promote self-help participation but where the treatment culture is naive to 12-step ideology. We also investigate factors predictive of active referral practices.

**Methods:** A cross-sectional survey was used to collect information about the attitudes, knowledge and referral practices toward TSG from 365 addiction treatment professionals in Norway in mid 2008 (80% response rate; N =291).

**Results:** Participants generally had positive attitudes toward TSG, but still 59.3 % of the clinicians did not refer any clients to TSG in the past week. In logistic regression, familiarity with the 12-step ideology, higher self-efficacy of making a successful referral and higher knowledge about the TSG were associated with greater odds of referring patients.

**Conclusions:** Referral to TSG in this Norwegian sample of clinicians was low, as was knowledge about TSG. Given empirical evidence about the usefulness of TSG to promote recovery, and Norwegian health authorities' stated goal to integrate self-help groups in health services, findings point to the need for training to raise awareness, knowledge about and referral to TSG among Norwegian substance abuse clinicians.

**Support:** The study was funded by the Research Council of Norway.

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**THE EFFECTS OF MARIJUANA ON CREATIVE PROBLEM SOLVING.**

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**Aims:** Individuals who smoke marijuana (MJ) often claim to experience enhanced creativity while smoking, including increased concentration and ability to generate unique ideas. However, this relationship has not been empirically demonstrated. Our initial pilot study in near-daily MJ smokers revealed that there were no effects of MJ (3.98% THC) on creative problem solving, as measured by divergent thinking tasks (tasks that ask participants to generate as many ideas as possible to a presented problem), yet subjective ratings of task performance improved after MJ administration. The present pilot study sought to determine if there were dose-dependent effects of MJ on creative problem solving (divergent thinking tasks) in MJ smokers.

**Methods:** Twenty-five healthy participants (17M, 8F) who reported smoking MJ 4 ± 2 days each week completed these tasks as part of a within-subject study on MJ and risk taking. MJ cigarettes (0.0, 1.98, 3.98% THC) were administered in systematically varied order using a standardized paced-puffing procedure in 3 separate laboratory sessions. Creativity tasks were completed at baseline and approximately 20 min after MJ smoking to capture peak drug effects.

**Results:** Repeated measures ANOVA with planned contrasts suggested a marginal improvement in fluency (number of ideas) after the 1.98% THC MJ concentration was smoked ( $15.15 \pm 7.3$  vs.  $17.36 \pm 9.10$ ,  $p=.06$ ). There were no differences in flexibility (number of categories of ideas) as a function of MJ concentration. Individuals rated their ideas as more "funny" ( $p=.06$ ) and "elegant" ( $p=.05$ ) after smoking the 1.98% THC concentration, while ratings of how "well" they performed increased after the 3.98% concentration ( $p=.03$ ) compared to placebo MJ.

**Conclusions:** These data, which suggest that MJ improves perception of performance without robustly improving objective measures of creative problem solving, have potential clinical implications: daily MJ smokers often state they smoke MJ to improve their creativity. Future research should confirm this finding using other types of divergent thinking tasks, such as those with more real world applicability.

**Support:** P50 DA09236

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**ASSESSMENT OF INDIVIDUAL DIFFERENCES IN THE AVERSIVE AND REWARDING EFFECTS OF MORPHINE.**

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**Aims:** Although drugs of abuse produce both rewarding and aversive effects, few studies have examined the relationship between these effects in individual subjects to determine if they are mediated by a common mechanism. To this end, the present study examined the ability of morphine to induce both place preferences and taste aversions using a combined conditioned taste aversion/conditioned place preference procedure.

**Methods:** Male Sprague-Dawley rats ( $n=40$ ) were given 20-min access to saccharin (0.1%) followed by a subcutaneous injection of morphine (5mg/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 4 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:** A 2x5 repeated measures ANOVA on saccharin consumption revealed effects of Group and Trial and a Group x Trial interaction ( $p's < 0.001$ ), indicating that animals treated with morphine readily acquired taste aversions (on Trials 2-5). Paired Samples t-test showed that the subjects administered morphine also acquired place preferences ( $p's < 0.05$ ), spending more time in the drug-paired chamber on Trials 1-4. Although both effects were conditioned, there was no relationship between the strength of place preference and strength of taste aversion on any trial (Pearson Correlation  $r's \leq 0.363$ ,  $p's \geq 0.116$ ).

**Conclusions:** Although morphine has both rewarding and aversive effects (as assessed by the place preference and taste aversion designs, respectively), these effects appear unrelated, suggesting that these two affective properties of morphine are mediated by different mechanisms.

**Support:** Supported by a grant from the Mellon Foundation to AV and ALR.

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**DRUG USE IN INDIVIDUALS SCREENED FOR PARTICIPATION IN HUMAN BEHAVIORAL PHARMACOLOGY LABORATORY STUDIES.**

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**Aims:** National data suggest that drug use peaks in the late teens and early twenties. This study sought to determine if this trend holds true for individuals undergoing screening to participate in human behavioral pharmacology studies

**Methods:** Intake data were examined for 192 (46 female) subjects aged 18-50, screened during a one-year period (11/01/2007-10/31/2008) to participate in studies based at the University of Kentucky Laboratory of Human Behavioral Pharmacology. Outcome variables included age, positive drug urine screens and recent self-reported drug use. Data were analyzed using descriptive statistics. We hypothesized that drug use would be most prevalent in younger subjects.

**Results:** Urine toxicology results indicated recent drug use in 40% (ages 40-44) to 80% (ages 30-34) of individuals. Positive urines were most likely to indicate recent marijuana or cocaine use. An even greater percentage of screened subjects self-report drug use in the past 30 days, from 80% (ages 18-20) to 100% (ages 30-34). Interestingly, the drugs used in the past 30 days differed across age groups. Younger individuals reported recent amphetamine use whereas older individuals reported recent cocaine use. Recent use of other drugs was relatively even across age groups.

**Conclusions:** Overall, the individuals screened for participation in these studies reported greater levels of drug use than those observed in national epidemiological data. The highest rates of drug use were observed in those aged 30-34, which is also different from what has been reported from national data sets. These data suggest that individuals screened for human behavioral pharmacology studies are more likely to be drug-experienced than the general population.

**Support:** Grants R01 DA010325, 017711, 020429, 021155 (CRR) and R21 DA0204089 (WWS).



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**ANTINOCICEPTIVE AND MOTORIC EFFECTS OF I.C.V. THC IN MALE VS. FEMALE RATS.**

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**Aims:** Previous research has shown that systemically administered cannabinoids produce greater antinociceptive effects in female compared to male rats. The aim of this study was to examine whether sex differences are due to supraspinal mechanisms.

**Methods:** Vehicle (1:1:8 ethanol:cremaphor:saline) or  $\Delta$ -9-tetrahydrocannabinol (THC, 100  $\mu$ g) was administered into the right lateral ventricle (i.c.v.) of adult male and female Sprague-Dawley rats (N=6/sex/dose). Antinociception was measured using paw pressure and warm water tail withdrawal tests at 5-240 min post-injection. Horizontal locomotion was examined in 5-min periods at 15-240 min post-injection, and catalepsy was measured at 30 min post-injection.

**Results:** THC produced peak antinociception at 15 min post-injection on both tests, returning to baseline levels at 90-120 min post-injection (paw pressure: THC x time,  $P=0.001$ ; tail withdrawal: THC,  $P=0.002$ ). THC reduced locomotor activity 15-30 min post-injection (THC x time,  $P=0.025$ ). THC did not produce significant catalepsy. No sex differences were observed on any measure, except THC produced a second peak of paw pressure antinociception at 90 min post-injection in females only.

**Conclusions:** These results suggest that sex differences in behavioral effects of systemically administered THC are not mediated by supraspinal mechanisms. The second peak in paw pressure antinociception that occurred only in females may reflect the production of THC metabolites, which we have previously shown is greater in female than in male rats.

**Support:** This research was supported by a grant from the Peter F. McManus Charitable Trust.

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**RELAPSE AND RECOVERY AMONG HEPATITIS C-INFECTED PATIENTS WITH A HISTORY OF COCAINE OR HEROIN USE.**Alexander Y Walley<sup>1</sup>, T Heeren<sup>2</sup>, C Bliss<sup>2</sup>, P R Skolnik<sup>1</sup>, S Stuver<sup>2</sup>, D Nunes<sup>1</sup>, D Cotton<sup>1</sup>; <sup>1</sup>Boston University School of Medicine, Boston, MA, <sup>2</sup>Boston University School of Public Health, Boston, MA

**Aims:** Among hepatitis C (HCV)-infected outpatients with prior heroin or cocaine use, we describe transitions between active heroin or cocaine use, treatment, and abstinence and identify factors associated with relapse and recovery.

**Methods:** We studied subjects enrolled in CHARM, a longitudinal cohort study of HCV-infected outpatients interviewed every 12 months, with prior heroin or cocaine use and at least 2 follow-up interviews. At each interview, subjects were classified into one of 5 states: a) active use b) recent detoxification c) residential treatment d) methadone or suboxone treatment e) abstinence without treatment. We categorized intervals of consecutive follow-up interviews as "recurrent use" (e.g., active use to active use), "recovery" (e.g., active use to abstinence), "maintenance" (e.g., abstinence to abstinence) and "relapse" (e.g., abstinence to active use). Using logistic regression with generalized estimating equations, we determined associations between homelessness, alcohol use, and incarceration as time-varying independent variables and recovery vs. recurrent use and relapse vs. maintenance as outcomes.

**Results:** Among 364 subjects with a mean of 3.4 follow-up visits, at least once during follow-up 11% had a recurrent use interval, 29% had a recovery interval, 87% had a maintenance interval and 24% had a relapse interval. In adjusted models that included age, gender, race, HIV coinfection, subjects with homelessness (OR 3.28; 95%CI: 1.28-8.38), alcohol use (OR 3.09; 95%CI: 1.98-4.84), and incarceration (OR 3.49; 95%CI 1.90-6.40) were more likely to have a relapse than a maintenance interval. No significant differences were detected in adjusted models for recurrent use vs. recovery intervals.

**Conclusions:** Among HCV outpatients with prior heroin or cocaine use, most are abstinent or in treatment most of the time, but relapses and recoveries are common. Relapse prevention strategies should include focused efforts for patients with homelessness, alcohol use and recent incarceration.

**Support:** NIDA R01 DA019841 D. Cotton, PI.

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**PSYCHOSTIMULANT BEHAVIORAL AND NEUROCHEMICAL EFFECTS ARE MORE RAPID IN ADOLESCENT THAN ADULT RATS.**

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**Aims:** Most drug addictions begin in adolescence and the time from first use to dependence appears to be less in adolescence. Our work in rats showing that cocaine and other DAT inhibitors induce more ambulatory behavior and electrically-stimulated dopamine release suggests biologic differences in dopamine system maturation might contribute to the adolescent addiction vulnerability in humans. Drugs, formulations and routes of administration that produce the most rapid drug accumulation in brain are most addictive. The current studies tested whether this phenomenon of rapid onset of drug action is characteristic of adolescent rats after psychostimulant drug administration.

**Methods:** Ambulatory behavior was determined at one minute intervals following i.p. injection of 1 mg/kg amphetamine, 10 mg/kg cocaine, 10 mg/kg methylphenidate and 5 mg/kg GBR12909 to rats on PN 28, 42 and 65. In separate groups of animals (PN 28 and 65) we examined electrically-evoked dopamine release in vivo using fast cyclic voltammetry at carbon-fiber electrodes placed in the dorsal striatum. Drug-enhanced dopamine release induced by 20 Hz stimulations were evaluated at 2.5 min intervals following i.p. injections.

**Results:** Ambulatory stimulation occurred significantly earlier in the youngest adolescent males following amphetamine and cocaine injection (<5min) but not following methylphenidate or GBR12909. Cocaine, amphetamine and methylphenidate stimulated dopamine release earlier in the adolescent than adult rat.

**Conclusions:** The present results suggest that the addictive psychostimulants stimulate behavioral effects earlier in the adolescent male rat, while all the stimulants tested increased dopamine release earlier in the adolescent regardless of reported addiction liability. The earlier effects in adolescents could reflect in part age differences in the dopamine system that support more pronounced increases at low, increasing drug concentrations in tissue.

**Support:** Supported by DA019114.

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**EARLY CHILDHOOD AGGRESSIVE BEHAVIOR, INITIAL TOBACCO EXPOSURE OPPORTUNITY AND TRANSITION FROM OPPORTUNITY TO FIRST TOBACCO USE: A PROSPECTIVE STUDY IN URBAN AFRICAN AMERICAN YOUTH.**Yan Wang<sup>1</sup>, N S Ialongo<sup>2</sup>; <sup>1</sup>School of Medicine, University of Maryland at Baltimore, Baltimore, MD, <sup>2</sup>Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

**Aims:** Aggressive behavior in early childhood has been reported to elevate the risk of initiation of drug use among youth (Kellam et al., 1980; Brook et al., 1992). Exposure opportunities to try drugs and transition from initial drug opportunity to first drug use are two important stages of the earliest drug involvement (Van Etten & Anthony, 1997; Wagner et al., 2002). However, it is not clear how aggressive behavior affects the two stages of onset of drug use, separately. To fill the gap, this study prospectively examined initial tobacco exposure opportunity and first tobacco use once given opportunity as a function of aggressive behavior in first grade and examined the possible gender variations.

**Methods:** The original sample from a preventive intervention trial included 678 urban first-graders who participated in two school-based intervention trials and were followed up to one year beyond anticipated high school graduation. For analyses on initial exposure opportunity, the sample was restricted to the 660 youth who had never smoked by grade 1. For analyses on first tobacco use once given opportunities, the sample was further restricted to the 443 youth with opportunities to try smoking within the 12 years following grade 1. Discrete-time survival analysis was conducted with Mplus software.

**Results:** Aggressive behavior was related to a modestly greater hazard of first tobacco use once given opportunities to try tobacco (aHR:1.3, 95% CI: 1.1-1.5,  $p=0.001$ ), but was not significantly related to the first tobacco exposure opportunity. No significant gender variation was found in the relationships.

**Conclusions:** This study suggests that tobacco prevention strategies should focus on prevention of the youth, including boys and girls, from being exposed to drugs and also prevention of them from transition to drug use once exposed, especially among those with elevated aggressive behaviors.

**Support:** NIMH (R01MH57005) and NIDA (R01DA11796).

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# TRANSACTIONAL MULTIPLE RISK MODEL: INTERACTIVE EFFECTS OF GENDER, ENVIRONMENTAL RISK, AND PRENATAL COCAINE EXPOSURE ON DEVELOPMENTAL OUTCOMES FROM BIRTH TO ADOLESCENCE.

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**Aims:** Research on the developmental effects of prenatal cocaine exposure indicated that the adverse cocaine effects tend to be subtle and small and that boys tend to be more vulnerable to cocaine effect. Environmental risk has been identified as a confounding variable that has not been systematically studied from a longitudinal perspective. In this research program, we use a transactional multiple risk model to examine main and interactive effects of gender, environmental risk, and prenatal cocaine exposure on developmental outcomes throughout childhood into adolescence. Developmental outcomes of particular interest include behavioral inhibition, emotional regulation, psychological adjustment, peer relation, and risk taking behaviors.

**Methods:** Not required

**Results:** Not required

**Conclusions:** This research program will generate new knowledge on this unique population. It will contribute to the translation of theory and research into intervention practices. We have a unique opportunity to make this new research program feasible. That is, our ongoing longitudinal study is one of the only two NIDA-funded longitudinal projects that follows a cohort of newborns with prenatal drug exposure and a matched control group through adolescence. Leveraging the existing resources to further advance our research endeavor is particularly critical under the current finance situation in the nation.

**Support:** NIDA funded

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# LOW EDUCATIONAL ATTAINMENT AND CIGARETTE SMOKING DURING PREGNANCY.

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**Aims:** Low educational attainment is a robust predictor of chronic health problems and a significant risk factor for cigarette smoking and other substance use disorders. This study examined the influence of educational attainment on smoking status in a cohort of pregnant women who were cigarette smokers at conception.

**Methods:** Study participants (n = 316) were subjects in clinical trials examining voucher-based contingency management for smoking cessation and relapse prevention. Multivariate analyses were used to examine whether educational attainment (< 12 yrs., 12 years, and > 12 years) predicted (a) smoking status at the start of prenatal care, (b) outcome of antepartum smoking-cessation therapy, and (c) relapse back to smoking 6-months postpartum.

**Results:** Educational attainment was a robust predictor. Compared to women who attained < 12 years of education, those with > 12 years of education were 27.2 times more likely to quit smoking before entering prenatal care, 2.8 times more likely quit when provided treatment, and 5.7 times more likely to remain abstinent at 6-months postpartum. In addition to educational attainment, other predictors of smoking status included treatment condition (abstinence-contingent vs. noncontingent voucher delivery), smoking-related characteristics (e.g., # of cigarettes/day smoked pre-pregnancy), maternal age, and stress ratings.

**Conclusions:** Strategies to increase educational attainment should be included with more conventional tobacco-control policies in efforts to reduce smoking among girls and women.

**Support:** R01DA14028 and T32DA07242 from NIDA

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# MODERATORS OF THE RELATIONSHIP BETWEEN RISK TAKING PROPENSITY, SUBSTANCE USE, AND OTHER RISK BEHAVIORS IN EARLY ADOLESCENTS.

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**Aims:** Ample research suggests that risk taking propensity, or reward seeking, is related to risk behaviors including substance use in youth and adulthood. However, few studies have explored the function that negative reinforcement may serve in the emergence of such behaviors. Additionally, studies have not considered the potential effect of environmental factors, such as father absence, with risk taking propensity on early adolescent substance use and risk behavior. Thus the aim of the current study was to examine cross-sectionally the link between risk-taking propensity and behavioral distress intolerance as an index of negative reinforcement with real world risk-taking behavior in pre-adolescents.

**Methods:** This cross-sectional study examined distress intolerance and father absence as moderators in the relationship between risk taking propensity and risk (i.e., substance use, delinquency, and safety behavior) in a community sample of 244 youth (mean age = 12.1 years, 45% female, 50% White). Youth completed the CDC Risk Behavior Survey, the Balloon Analogue Risk Task-Youth, the Behavioral Indicator of Resiliency to Distress, and the Brief Sensation Seeking Scale. Parents completed one Father Absence item.

**Results:** Controlling for age, gender, and sensation seeking, findings showed no significant main effects for father absence, risk taking, or distress intolerance. However distress intolerance and father absence both separately moderated the link between risk taking propensity and real world risk behavior engagement.

**Conclusions:** Findings indicate that risk taking propensity is related to real world risk taking behaviors among those with high levels of distress intolerance and who reside in a home where the biological father is absent. These results have implications for understanding the roles negative reinforcement and family contextual processes play between youth risk propensity and real world risk engagement.

**Support:** NIDA Grant R01 DA18647

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# WORKFORCE DEVELOPMENT FOR FAITH-BASED SUBSTANCE ABUSE TREATMENT PROVIDERS.

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**Aims:** Faith-based leaders, counselors, and other staff enrolled in a technology transfer workshop series participated in a needs assessment to identify training needs and barriers.

**Methods:** Pacific Southwest Addiction Technology Transfer Center partnered with Los Angeles Metropolitan Churches and the African American Alcohol and Other Drug Council to perform an extensive needs assessment to obtain basic descriptive characteristics to inform the training needs of sixty-five (65) respondents.

**Results:** Selected highlights revealed that: Sixty-six percent (66%) were female; median age was 50; 72% were African American; 54% were in recovery; 60% endorsed addiction counseling as their profession; 34% had worked 1 to 4 years in the mental health field; 48% had worked in their current agency for 1 to 4 years; 42% had some college; 72% identified providing comprehensive care for dually diagnosed clients has a training need; and 43% felt budget and limited resources (37%) were main barriers to receiving training.

**Conclusions:** Faith-based providers in community settings are an under utilized workforce that have tremendous potential to deliver state of the art substance abuse counseling once their training needs are identified, and training is then customized to address these issues.

**Support:** HHS/SAMHSA/CSAT Grant Number:5UD1 TI013594-07

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**COULD LOW DEPENDENT SMOKERS BE MORE CUE REACTIVE THAN HIGH DEPENDENT SMOKERS?**

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**Aims:** Cue reactivity procedures are well-established methods to examine craving and stimulus control. For smokers, the relationship between nicotine dependence and cue reactivity has not been clearly established. Within a recently completed parent study of gender and hormonal effects on lab-based measures of cue reactivity, our aim was to examine this relationship further.

**Methods:** Participants (N=90) ages 18-40 smoking >10 cigarettes per day were eligible for study entry. Average nicotine dependence (Fagerström Test of Nicotine Dependence; FTND) at baseline was 4.9 (SD=2.1). Participants completed a cue reactivity session consisting of two in vivo cues (smoking, neutral) and two affective imagery cues (stressful, relaxed), all counterbalanced. Craving in response to cues was assessed following each cue exposure using the Questionnaire of Smoking Urges (QSU). Cue reactivity was operationally defined as the difference in QSU scores between the in vivo and neutral cues, and between the stressful and relaxed cues.

**Results:** Results showed that FTND was negatively associated with hedonic craving (QSU Factor 1) for imagery cues, such that those who had low FTND scores demonstrated greater cue reactivity than those with higher FTND scores ( $\beta = -.263$ ;  $p = .012$ ). Similar associations were found for other QSU measures (Total & Factor 2) and for in vivo cues, but did not reach statistical significance.

**Conclusions:** Under some circumstances, smokers with lower levels of nicotine dependence may be under greater stimulus control and thus more cue reactive than smokers high in nicotine dependence. It may be that high dependent smokers exhibit high levels of craving regardless of cue exposure, thus dampening their differential reactivity to laboratory cues. These findings may have implications for participant selection and analysis in future studies of smoking cue reactivity.

**Support:** Supported by NIDA (P50DA016511, K23DA020482, K12DA000357) and USPHS (M01RR01070).

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**DOUBLE JEOPARDY FOR DRUG-USING WOMEN IN RUSSIA: INJECTING AND SEXUAL RISKS REPORTED IN A SMALL TRIAL.**

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**Aims:** Female drug injectors in Eastern Europe are at risk for HIV through heterosexual contact and injecting behaviors. This study examines the first baseline questionnaires (n=57) of women enrolled in a NIDA supplement to adapt and test the Women's CoOp—a "best-evidence" woman-focused HIV prevention intervention—with female injectors detoxifying in the Leningrad Regional Center of Addictions. Sexual and injecting risks, and the intersection of impaired sex are presented.

**Methods:** Women aged 18 to 30 who reported injecting drugs during the past year and are currently in substance abuse treatment were enrolled in a randomized trial aimed at reducing HIV risk.

**Results:** The average age of participants was 26. Alarming high rates of HIV were found (59%), with early onset of injecting drug use (mean age 18), combined alcohol and injecting drug use (54.4%), high levels of current injecting frequency (mean 97/month), and 46% having shared injecting works. Almost a third reported trading sex for drugs, money, clothing, shelter or other goods, and sex with a main partner to get heroin injected. These women also reported unprotected sex with their main partner about half the time and 58% reported unprotected vaginal sex at last sex act. Among participants, 88% reported being impaired during sex, with 35% of their partners having used heroin before or during last sex act.

**Conclusions:** Early onset of injecting drug use, unsafe injecting drug practices, and unsafe sex practices while impaired puts these women at high HIV risk, as shown by the prevalence rates. In addition, many reported that their partners also use drugs. Behavioral interventions to reduce drug use and empower women to adopt safer sex and drug use practices are urgently needed in Russia where no methadone or substitute therapy is available and detoxification becomes a revolving door.

**Support:** This research was supported by NIDA grant RO1 DA11609.

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**GENDER DIFFERENCES IN EMPLOYMENT AND EMPLOYMENT BARRIERS AMONG DRUG ABUSERS.**

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**Aims:** Drug users often face periods of unstable employment. Early studies found that stable employment plays an integral and supportive role in drug and alcohol treatment retention, and Vaillant (1988) concluded that an unstable employment history was a better predictor of relapse than addiction severity.

Most of the research on employment among drug abusers has been conducted with community treatment populations; fewer studies have examined the relationship between employment and treatment outcomes in criminal justice samples despite the particularly high rates of drug use in this population. In general, employment is viewed by treatment providers and others in criminal justice settings as a "gateway" into new, healthy, and productive social and professional relationships for drug users; however, criminally-involved drug abusers face additional barriers to employment and females may be especially limited by these challenges.

This research group completed a randomized controlled trial of a promising employment intervention for drug court participants and is now adapting the intervention for delivery via the Internet to further examine gender differences in employment and employment barriers among drug-abusing offenders. Special emphasis will be placed on collecting data to identify and examine important gender differences in employment, barriers to employment, and perceptions of work as well as to understand gender differences in experiences with the Web-based intervention.

**Conclusions:** Results from the Internet-based employment intervention will fill gaps in our knowledge about employment barriers, experiences, and attitudes toward employment as they relate to gender. In addition, the findings will have implications for other interventions as technology's role in the treatment of drug abuse and related problems continues to grow.

**Support:** This research is supported by a grant (R21 DA021178) from the National Institute on Drug Abuse to Matthew Webster.

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**INCREASED REWARD THRESHOLDS ("DYSPHORIC"-LIKE STATE) IN RATS WITH EXTENDED ACCESS TO METHAMPHETAMINE SELF-ADMINISTRATION.**

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**Aims:** Previous research showed that extended access to cocaine produced increased cocaine intake that was correlated with increased intracranial self-stimulation (ICSS) thresholds in rats, which suggests a dysphoria-like state in rats with extended access to cocaine. In the present experiment, we tested the hypothesis that rats self-administering methamphetamine with extended access would show similar escalation in intake paralleled by increased ICSS thresholds. Additionally, the effect of D2 dopamine receptor partial agonists on ICSS thresholds at various stages of methamphetamine self-administration was examined.

**Methods:** Specifically, the effects of terguride and aripiprazole on ICSS thresholds were first measured in drug-naïve rats. Then, the rats self-administered methamphetamine (0.05 mg/kg/injection) under a fixed-ratio 1 schedule with one-hour access for 11 days, then with six-hour access for another 11 days, during which ICSS thresholds were measured one hour before (17 hours post-methamphetamine self-administration) and three hours after daily methamphetamine self-administration. The effect of terguride on ICSS thresholds in rats was determined at the end of each access condition.

**Results:** ICSS thresholds remained stable during methamphetamine self-administration with one-hour access. However, during methamphetamine self-administration with six-hour access, ICSS thresholds gradually increased, and the increase in ICSS thresholds correlated with the increase in methamphetamine intake. The D2 receptor partial agonists tested here increased ICSS thresholds in rats regardless of different histories of methamphetamine self-administration.

**Conclusions:** The data suggest that a dysphoria-like state develops with extended access to methamphetamine in rats and may be a useful model of the dependence associated with methamphetamine addiction.

**Support:** (Supported by NIDA grants DA-10072 to G.E.K.)

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# A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL OF SELEGILINE HYDROCHLORIDE FOR SMOKING CESSATION: PRELIMINARY RESULTS.

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**Aims:** The primary aim of this study was to determine the safety and efficacy of the MAO-B inhibitor selegiline hydrochloride (L-Deprenyl; Eldepryl) as an aid for smoking cessation.

**Methods:** N=101 nicotine dependent community-dwelling adult cigarette smokers participated in this 8-week randomized, double-blind, placebo-controlled trial. Participants received either selegiline hydrochloride (DEP, 5 mg bid, n=51) or placebo (PLO, n=50) and brief (<10 minutes) manualized smoking cessation counseling. The main outcomes measures were 7-day point prevalence at end of trial (EOT), 4-week continuous smoking abstinence at end of trial (CA), and 7-day point prevalence abstinence at 6 month follow-up (6MFU).

**Results:** Participants did not differ by medication group on baseline smoking variables, age, or gender. The medication groups did differ on racial composition ( $p<0.05$ ). Treatment retention and medication compliance was high and not significantly different between DEP and PLO. Rates of smoking abstinence did not differ by medication group (EOT: DEP=20%, PLO=28%,  $N=101$ ,  $p=0.32$ ; CA: DEP=18%, PLO=24%,  $N=101$ ,  $p=0.43$ ; 6MFU: DEP=16%, PLO=17%,  $N=87$ ,  $p=0.89$ ). Adverse events were modest and comparable between study medication groups. Participants in the DEP group were more likely than PLO to report dry mouth (25.5% versus 8.2%,  $p<0.05$ ).

**Conclusions:** Our results suggest that selegiline hydrochloride was safe and well-tolerated by adult smokers, but did not improve smoking abstinence rates compared to placebo.

**Support:** Supported in part by grants R01-DA-15757 and K02-DA-16611 (to TPG) and K12-DA-00167 (to AHW) from the National Institute on Drug Abuse (NIDA), and the Endowed Chair in Addiction Psychiatry from the University of Toronto (to TPG).

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# "FOR MY DAUGHTER": INTERPERSONAL MOTIVATORS OF HEROIN CESSATION IN A COMMUNITY-BASED SAMPLE.

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**Aims:** We sought to examine the significance of interpersonal connections as motivator of cessation among former and relapsed heroin users participating in qualitative interviews as part of the CHANGE study of drug cessation. We hypothesized that emotional ties to non-users may promote and support recovery efforts.

**Methods:** In-depth interviews, focused on drug use and drug cessation, were conducted with 20 former and 12 relapsed heroin users. Interviews were audio-taped and transcribed. Coding of 18 interviews has been completed, using pre-identified and emerging themes. Analysis was done as a collaborative and iterative process involving study interviewers, coders and investigators.

**Results:** Participants were primarily male (72%) and black or Latino (94%); over half were age 39+. Socioeconomic status was low: 44% of the sample did not have a HS diploma/GED; 41% were homeless. Exposure to childhood and adult trauma was common. Personal motivators for cessation, including desired improvements in health, housing and finances, were described by a number of study participants. Interpersonal connections, primarily to parents and children, were, however, more common. Family members and others provided negative pressure to stop drug use, including criticism and restrictions on financial support. More significant, were tangible as well as abstract concerns regarding these important relationships. Statements such as, "I have feelings for him, and I actually did it for him" reflect participants' desire to rebuild or maintain ties to family and friends. Other statements, including, "In my heart it was my [late] mother watching over me and [me] feeling so guilty," demonstrate self-imposed pressures related to respect, image and a desire to live in accordance with the values of loved ones.

**Conclusions:** Emotional connections to family members and other loved ones were important motivators for cessation in our sample of former and relapsed heroin users. Drug treatment that builds on these sentiments may promote the recovery goals of clients.

**Support:** National Institutes of Health (Grant #: DA022123)

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# USE OF AN ADAPTIVE TREATMENT RESEARCH DESIGN IN A CTN STUDY OF PRESCRIPTION OPIOID DEPENDENCE TREATMENT.

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**Aims:** The NIDA Clinical Trials Network is conducting the Prescription Opioid Addiction Treatment Study (POATS). This 10-site trial examines different lengths and intensities of buprenorphine and drug counseling for subjects with opioid analgesic dependence. The primary study aim is to determine whether adding counseling to buprenorphine plus medical management improves outcome in this population during Phase 1, an initial 4-week taper, and Phase 2, a subsequent 12-week stabilization treatment for those who relapsed during or soon after Phase 1.

**Methods:** This study, which has completed recruitment (N=653), employs an adaptive treatment research design (ATRD); in an ATRD, subjects receive an initial treatment (pre-specified or randomly assigned), with a plan to evaluate treatment response and potentially make clinical adjustments when a pre-specified time point or clinical status (e.g., remission or relapse) is reached. In POATS, subjects with poor outcomes in Phase 1 enter Phase 2, at which time they are randomized to a new treatment. ATRDs have been used to study a number of disorders (e.g., depression), but they have been used infrequently in drug abuse studies.

**Results:** Advantages of an ATRD include 1) the ecological validity associated with a study designed to approximate real-world clinical practice (i.e., instituting one treatment, then trying something else if the first treatment fails), and 2) the ability to answer multiple research questions in one study. Thus, POATS is evaluating a treatment strategy, rather than a discrete treatment intervention. Major challenges include 1) determining and masking from subjects the behavioral criteria that trigger randomization into Phase 2, and 2) powering a study when only a subset of the original population will enter the second phase of the trial.

**Conclusions:** Designing and conducting a drug abuse study with an ATRD has both advantages (e.g., ecological validity) and associated challenges (e.g., masking).

**Support:** NIDA Grants DA15831, DA022288, DA022297, DA013045, DA020036

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# INTERACTION OF S1P AND FTY720 WITH OPIOID SYSTEMS IN THE PRODUCTION OF ANTINOCICEPTION AND OPIOID TOLERANCE.

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**Aims:** Sphingosine-1 phosphate (S1P) receptors are similar to cannabinoids in their activity and localization in the CNS. Since we observe cannabinoid/opioid interactions, we evaluated the potential interaction of S1P receptor activation with opioids.

**Methods:** Using the tail-flick test for antinociception, the Martin tetrad in both normal and transgenic mice, and the activation of G proteins, we evaluated the interaction of the S1P and opioid systems.

**Results:** S1P and an analog, FTY720, produce antinociception that is non-CB1, non-CB2 mediated, but is completely blocked by the opioid antagonists, naloxone and nor-BNI. S1P (icv.) produces antinociception in both ICR mice and wild type C57BL/6J mice. ED50 values for the ICR and C57 mice are 17.3 (11.9 - 25.2) versus 24.6 (10.8 - 55.8 micrograms/mouse, icv.), respectively. S1P is not active in CB1 receptor knockout mice and is 3-fold less potent in mu opioid receptor knockout (MOR) mice. The effects of S1P and FTY720 are also observed in the "Martin tetrad". FTY720 is active via the i.p. route of administration [ED50 = 2.3 (1.5 - 3.4) mg/kg]. S1P and FTY720 at inactive doses enhanced the antinociceptive effects of morphine significantly reducing the morphine ED50 by nearly 4-fold but are not cross-tolerant to morphine. FTY720 (2 mg/kg, i.p.) administered in conjunction with either morphine or placebo pellets implanted s.c. significantly blocked the development of tolerance to morphine. FTY720 (2 mg/kg, i.p.) also produced tolerance; morphine was not cross-tolerant to FTY720. Tolerance to FTY720 was observed in MOR mice and was accompanied by significant decreases in the activation of G-proteins in most brain regions.

**Conclusions:** Our data indicate that S1P analog/opioid therapy may produce long-term antinociceptive effects at doses devoid of substantial side effects, while preventing the neuronal biochemical changes that accompany tolerance (and perhaps physical dependence) to opioids.

**Support:** This work was supported by NIDA grant DA022581 and the Jeffress Memorial Trust.

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**IMPULSIVITY DOES NOT CORRELATE WITH WORKING MEMORY OR ALCOHOL PREFERENCE IN RATS BRED FOR ALCOHOL PREFERENCE.**

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**Aims:** The present study tested the hypothesis that differences in working memory in 3-pairs of alcohol preferring and non-preferring rat strains [inbred P and NP (iP and iNP), HAD1 and LAD1 (iHAD1 and iLAD1), and HAD2 and LAD2 (iHAD2 and iLAD2)] are due to differences in impulsivity.

**Methods:** Young adult, male iP/iNP, iHAD1/iLAD1 and iHAD2/iLAD2 rats, food deprived to 85% of their free feeding weights, were trained to respond under a FR50 schedule of food presentation. Upon completion of the 50th response, additional food pellets could be earned by withholding responses for increasing durations of time following the completion of each FR50. If the rat made a single response following the completion of the FR50, the next food pellet could only be earned by completing a FR50. Once the behavior stabilized, either saline or increasing doses of ethanol (0.5 – 1.75 g/kg) were administered, ip, 30 min prior to the start of the session. Sessions terminated after 1200 sec.

**Results:** Following saline administration, iP rats had a greater ability to withhold responses than iNP rats. There were no significant strain differences in any parameter following saline administration to the iHAD1/iLAD1 and iHAD2/iLAD2 rats.

Significant strain x dose interactions for the effect of ethanol in the iP/iNP rats resulted in a rightward-shift of the ethanol curve in the iP rats compared to the iNP rats. In the iHAD1/iLAD1 rats, the curve for ethanol in the iHAD1 rats fell to the left of the curve for the iLAD1 rats. Similar differences were not observed in the iHAD2/iLAD2 rats.

**Conclusions:** These results suggest that the iNP rats have less ability to withhold responses than the iP rats and therefore may be more impulsive. No such relationship was observed in the other four rat strains suggesting that increased impulsivity is not the explanation for the differences in working memory reported earlier in these strains.

**Support:** Supported by NIAAA grant 5 R01 AA014977.

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**QUALITATIVE DIFFERENCES IN THE SELF-ADMINISTRATION OF RATS RUNNING AN ALLEY FOR INTRA-PFC AND INTRA-NACC COCAINE.**

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**Aims:** Our laboratory has developed a runway model of drug self-administration in which rats are trained to run a straight alley once a day for a drug reinforcer delivered upon goal box entry. Rats running for i.v. or i.c.v. cocaine (but not other reinforcers) develop a unique pattern of approach-avoidance conflict about entering the goal box that has been shown to stem from the drug's mixed rewarding and anxiogenic properties. Since cocaine reinforcement has been attributed in large part to the drug's actions on the dopamine mesocorticolimbic system, it was of interest to determine whether the same pattern of mixed effects would be observed in rats running an alley for cocaine delivered directly into either of the two primary terminal regions of this system – the medial prefrontal cortex (mPFC) or the nucleus accumbens (NAcc).

**Methods:** Male rats stereotactically fitted with unipolar infusion cannula aimed directly above either the mPFC or NAcc were permitted to run the alley once a day (over 17 days) for a single infusion of cocaine (25µg/0.5µl injected over 80 s) or vehicle (artificial csf). This dose was based on prior work with i.c. and i.c.v. cocaine in runway and place preference studies. Run times (the time to cross the alley and enter the goal box) and approach-avoidance retreat behaviors (the number of stop-and-retreat responses that occur prior to goal box entry) were recorded for each rat on every trial.

**Results:** Results confirmed that rats running an alley for NAcc cocaine produced the same behavioral profile as reported for rats working for i.v. or i.c.v. cocaine – slowing run times associated with a distinct pattern of retreat behaviors that developed and strengthened over trials. In contrast, rats running for mPFC cocaine produced relatively fast run times and few retreats.

**Conclusions:** These data suggest that the positive and negative effects of cocaine are neurobiologically dissociable and that mPFC cocaine produces a more purely positive drug action than does NAcc cocaine.

**Support:** This work was supported by PHS grant DA05041 (AE).

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**CHRONIC MARIJUANA USERS HAVE DECREASED RESPONSIVENESS TO EMOTIONALLY CHARGED VISUAL STIMULI.**

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**Aims:** Recent studies have shown that acute Δ-9-THC exposure reduces normal amygdala reactivity to socially threatening stimuli in recreational marijuana users. The extent to which heavy marijuana exposure alters emotional information processing, however, remains unclear. The purpose of this study was to test whether chronic marijuana users (MJ Users) differ from controls (Controls) in brain function while viewing emotionally charged stimuli.

**Methods:** We collected event-related fMRI as MJ Users (N=12) and Controls (N=9) viewed and rated positive (40), negative (40) and neutral (20) photographs from the International Affective Picture System (IAPS). Based on individual ratings, we isolated the brain activity for each stimulus category. We compared the BOLD response between groups in several regions of interest (ROIs) known to be involved in processing emotional information.

**Results:** There were no difference between groups in the average (±SD) number of stimuli rated as positive (Controls = 36.3 ±6.3; MJ Users = 36.1 ±3.9), negative (Controls = 34.2 ±5.8; MJ Users = 33.8 ±4.6) or neutral (Controls = 27.3 ±6.7; MJ Users = 29.1 ±5.5). ROI analysis revealed that while viewing stimuli rated as positive, MJ Users had significantly less activity in the right amygdala and insula, compared to Controls. Similarly, while viewing stimuli rated as negative, MJ Users had significantly less activity in the right amygdala and left orbital frontal cortex, compared to Controls. There were no differences between groups in activity while viewing neutral stimuli.

**Conclusions:** These results demonstrate that chronic exposure to marijuana results in reduced responsiveness, as measured by the BOLD response, to positive and negative emotional stimuli. Reduced activity was found in the amygdala, as well as in the insula and orbitofrontal cortex, areas known to be involved in processing emotional information. These data suggest that heavy marijuana users may have difficulty in affective processing.

**Support:** NIDA grants DA007246 (MJW), DA020074 (LJP), and DA06634 (LJP)

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**AN INVESTIGATION OF SEXUAL PARTNERSHIPS AND HCV PREVALENCE AMONG REGULAR USERS OF COCAINE AND HEROIN.**

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**Aims:** Regular drug use is a known risk factor for increased morbidity and mortality. In recent years, empirical investigations have begun to examine how patterns of use influence infectious disease and social interactions, particularly sexual partnerships. With that in mind, the objective of this study was to examine the relationship between HCV prevalence and the number of casual sex partners among regular users of cocaine and heroin.

**Methods:** Study participants were adult injection and non-injection drug users enrolled in the Baltimore site of the International NEURO-HIV Epidemiologic Study, an epidemiological examination of neuropsychological, social, and behavioral risk factors of HIV, Hepatitis A Virus, Hepatitis B Virus, and Hepatitis C Virus. Separate regression analyses were conducted to examine the prevalence of HCV and to determine if there were links between that and other key covariates.

**Results:** There were 132 participants in the study sample; the mean age was 23.5 (SD = 3.6 years). After adjustment for age, gender, education, marital and ethnic category, results revealed that whites (OR = .20; CI = .06 - .69); males (OR = 1.33; CI = .45 - 3.90); individuals with less than a high school education (OR = 2.46; CI = 1.1 - 5.7) and those with more than 6 casual partners in their lifetime were all more likely to have HCV (OR = 2.4; CI = .99 - 5.7).

**Conclusions:** These preliminary findings contribute to existing literature which suggests that regular drug users with less than a high school education and their sexual partners may be more vulnerable to HCV and other sexually transmitted infections.

**Support:** Drug Dependence Epidemiology Training Program T32 DA007292 (PI: Dr. William Latimer)

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**RACE AND GENDER TRENDS OF CPDD MEMBERS AND MEETING ATTENDEES.**

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**Aims:** Background: CPDD leadership has placed increased attention since 1992 to improve membership diversity. The Underrepresented Populations Committee (URPOP) began collecting race and gender information of members in 2007. Objectives: (1) to assess the representation of racial minorities and women in CPDD; (2) to determine if there is a difference between CPDD members and annual meeting attendees; (3) to determine participation of racial minorities and women over time.

**Methods:** The dataset includes CPDD members from August 2008 (n=858) and CPDD annual meeting attendees from June 2008 (n=1,298). The dataset includes variables indicating member and attendee status, race, gender, membership level, year of membership, address, institutional affiliation, academic title, degree, and research interest.

**Results:** Preliminary descriptive analysis results show Caucasians make up 82.3 % of CPDD members with Asian Americans as the next largest group at 5.6%. African Americans and Hispanic or Latinos of any race are underrepresented at 2.2% and 5.4% respectively. For meeting attendees that are not members, Caucasians represent 62.2% and African Americans and Hispanics or Latinos respectively represent 5.4% and 11.2%. African American men make up 0.8% of members and 2% of annual meeting attendees, while African American women make up 3.6% and 7.0%. Caucasians make up 90.4% of Fellows and 84.1% of Regular Members. Since 1992, the representation of Caucasians has dropped from 93.9% of members to 82.3%. Women members have increased from 27.5% in 1992 to 47.4% in 2008.

**Conclusions:** There has been some improvement in the representation of racial minorities in CPDD membership. More racial minority representation is found among annual meeting attendees than members. The representation of women has greatly improved since 1992. The most disparity appears to be the underrepresentation of African American men and the promotion of racial minorities to the fellow level.

**Support:** Washington University School of Medicine discretionary funds.

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**ASSESSMENT OF A PROCESS IMPROVEMENT INITIATIVE IN SUBSTANCE ABUSE TREATMENT SETTINGS.**

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**Aims:** The Danya institute received funding from the Open Society Institute of Baltimore(OSI)to support the implementation of the Network for the Improvement of Addiction Treatment's (NIATx) six month Quality Improvement Capacity Building program, in 5 addiction treatment programs in Baltimore's Substance Abuse System (BSAS). The major goal of the NIATx program is to assist behavioral health programs in more effectively meeting the needs of consumers and the organizations that fund addiction treatment. The program provides the participating organizations with a systematic problem-solving approach that can help them, develop a deeper understanding of consumer needs; restructure the work flow to better respond to consumer and staff needs; and make the most efficient use of available resources. After going through the process improvement program, each of the organizations developed projects to address one of four key focus areas: reducing client waiting times, reducing client no-shows, increasing admissions, and increasing treatment length of stay. This study examines the usefulness and effectiveness of the process improvement program as well as the sustainability of changes made as a result of completing the program.

**Methods:** An online survey was sent to all participating members of the NIATx quality improvement process. The survey asked questions related to: the usefulness and effectiveness of the quality improvement process, the success or failure of each individual process improvement project, and the likelihood of using this model to address other areas of treatment program performance.

**Conclusions:** Results of this survey indicate that the improvement of general organizational processes can improve the overall functioning of substance treatment programs and potentially lead to better outcomes on state and federally mandated treatment indicators.

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**EXPERIENTIAL AVOIDANCE PREDICTS SUBSTANCE ABUSE TREATMENT ENTRY.**

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**Aims:** Experiential avoidance (EA) is an unwillingness to experience negative private events such as painful thoughts or emotions. It has been implicated in the etiology and course of many behavioral disorders including substance abuse (Hayes et al., 1996). However, the empirical relation between EA and substance use has not been clearly defined. The present study investigated: 1.the relationship between EA and treatment entry among 520 (26% female) substance dependent individuals (heroin 33.3%, cocaine 31.5%, marijuana 22.5%, and alcohol 10.2%) who presented for combined pharmacological and psychosocial treatment at an outpatient research facility and 2. treatment outcome among 133 participants (21% female) who entered a treatment study (37.6% heroin, 25.6% cocaine, 28.6 % marijuana, and 8.3% alcohol).

**Methods:** EA was assessed by the 10-item Acceptance and Action Questionnaire (AAQ-II) completed at the first clinic visit prior to participation in any treatment study. Scores on the AAQ-II can range from 10-70 with lower scores signifying relatively greater EA.

**Results:** Individuals entering treatment had a significantly ( $F(1,472)=9.558$ ,  $p=.002$ ) lower level of EA ( $M=42.8$ ,  $SD=11.7$ ) than those who did not enter treatment ( $M=38.8$ ,  $SD=12.1$ ). The odds of entering treatment significantly increased with lower levels of EA ( $\beta=.022$ ,  $p=.013$ ; 95% CI Odds Ratio = 1.01; 1.04). The relationship between treatment entry and EA was most pronounced among heroin dependent participants,  $r(163)=.179$ ,  $p=.023$ . Measures of treatment outcome (percent of treatment weeks completed, percent use, completer status, and drug responder status) were not found to be associated with EA.

**Conclusions:** EA may be an important factor in understanding the process of entering treatment, although its relationship to changes in drug use during treatment remains unclear. The implications of these findings for the measurement of experiential avoidance and for understanding its clinical utility in substance use treatment will be discussed.

**Support:** Supported by DA 021850

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**HIV RISK BEHAVIORS: RESULTS FROM A RANDOMIZED STUDY OF METHADONE MAINTENANCE FOR PRISONERS.**

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**Aims:** Aim: The goal of the Methadone Maintenance for Prisoners study was to examine the benefits of an intervention found effective in community settings, methadone maintenance, provided to a novel population – prison inmates who were nearing release. The current research examined baseline (30 days prior to most recent incarceration)and 1-month post-release differences in HIV risk behaviors.

**Methods:** Methods: Linear mixed model analyses were used to determine differences on selected items from the TCU AIDS Risk Assessment measure in 211 pre-release males with pre-incarceration heroin dependence who met criteria for methadone treatment. Participants had been randomly assigned to one of three conditions: 1) Counseling Only: counseling in prison without methadone and passive referral to community-based drug abuse treatment; 2) Counseling+Transfer: counseling in prison without methadone and with transfer to methadone maintenance in the community upon release; or, 3) Counseling+Methadone: counseling and methadone in prison with transfer to methadone treatment in the community upon release. Data were examined at study intake (Baseline, 30 days prior to the most recent incarceration) and post-release (1-month after release to the community).

**Results:** Results: Results showed there were no significant differences between treatment conditions over time. However, there were time differences regardless of treatment condition. The number of times drugs were injected with a needle significantly changed over time ( $p < .002$ ; Baseline  $M = 110.4$ ; SE: 10.5; 1 month  $M = 13.9$ ; SE: 2.7). Similarly, among sexual risk behaviors in the last 30 days there was a significant decline in unprotected sex over time ( $p < .001$ ; Baseline  $M = 19.4$ ; SE: 2.1; 1-month  $M = 8.8$ ; SE: 1.0).

**Conclusions:** Conclusions: Findings suggest that inmates are more likely to engage in risky drug use and sexual behaviors prior to incarceration. Upon release to the community it appears that their risky behaviors are decreased in the first 30 days.

**Support:** Supported by: RO1DA016237-01, Timothy Kinlock, PI.

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# NEW YORK DRUG POLICIES AND THE LIVED EXPERIENCES OF AFRICAN AMERICAN WOMEN IN DISTRESSED HOUSEHOLDS.

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**Aims:** Present a longitudinal qualitative analysis of the impact of New York's Rockefeller drug policies (Rock) on the lived experiences of three generations of African American women in distressed households drawing on standpoint and intersectionality theories. Distressed refers to a constant struggle with multiple crises precipitated by alcohol and/or other drug use or sale (AOD) including unemployment and poverty. Criminal justice, education, and welfare policies were also examined.

**Methods:** Two families were selected from two projects aiming to examine drug use/sales, violence, and family relationships. Selection criteria included impoverished families with data collected from 1995 to 2007 (N=11). Two family cases were selected to illustrate not just what happens in a single family, but how diverse the experiences can be.

**Results:** Participants developed a complex taxonomy of drug use and danger which contradict the assumptions in the Rock. Employment was one of the most significant factors in AOD desistance. Younger participants shunned crack/heroin use because they observed these drugs destroy their parents' lives. They consider marijuana/alcohol as safe/useful drugs as long as the user is able to provide for the household. Welfare, education, and criminal justice policies interacted creating an oppressive environment which made it difficult to thrive in mainstream society. For instance, coerced treatment was not applicable to participants' reality because it did not provide effective tools in dealing with the oppression and violence they experienced in their communities. Such treatment was perceived as a "vacation" from use and a tool to avoid incarceration or losing their children.

**Conclusions:** Findings inform researchers, practitioners, and policy makers in designing better AOD treatment that addresses the entire social reality of specific drug users. Consulting with community advocates may be critical in developing trust, engaging clients, and fostering community involvement at the legislative level.

**Support:** Supported by National Institute on Drug Abuse

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# QUALITY OF LIFE IN INPATIENTS UNDERGOING AN OPIOID MAINTENANCE THERAPY AFTER RELEASE FROM AN ADDICTION CLINIC.

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**Aims:** The concept of quality of life (QoL) is a multidimensional, complex and latent construct which serves to determine individual satisfaction with life in certain aspects and domains (Arpinelli & Bamfi, 2006). Within the field of addiction QoL turned out to be an appropriate indicator for measuring the effectiveness of maintenance treatment (Giacomuzzi et al. 2006). QoL in a cohort of 269 opioid-dependent patients meeting DMS-IV criteria for opioid dependence constituted the focus of our research.

**Methods:** Using a retrospective cohort study design, patients who had been in synthetic opioid maintenance therapy between 1998 and 1999 at the Addiction Clinic and then were discharged to general practitioners, were enrolled. Structured interviews (Addiction Severity Index, Quality of Life Questionnaire) and urine analysis at time of interview were conducted. All subjects gave informed consent and the study was approved by the local ethics committee.

**Results:** After 6 mailings, 85 (31.6%) patients were interviewed. From these 76.5% (N= 65) were still enrolled in maintenance therapy, 18.8% (N=16) were drug free and 4.7% (N=4) relapsed. 80% (N=68) of interviewed subjects categorized their quality of life as satisfying up to good. 47% (N= 40) reported to be satisfied with their life in general while 20% (N=17) were dissatisfied. Abstinent people (N=16) did not show greater satisfaction in any aspects of QoL than stable subjects in maintenance therapy (N=34). In 3 particular aspects of QoL, unstable patients in maintenance therapy (N=31) displayed poorer satisfaction in life than stable subjects in maintenance therapy (N=34).

**Conclusions:** Present results emphasize the beneficial effects of maintenance therapy on QoL among opioid dependent patients. According to our results abstinence is not associated with higher QoL when compared to stable patients in maintenance therapy.

**Support:** The study was supported by the OENB, Jubilaeumsfonds project No. 11650.

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# A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF OSMOTIC-RELEASE METHYLPHENIDATE IN INITIATING AND MAINTAINING ABSTINENCE IN SMOKERS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

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**Aims:** To evaluate the efficacy and safety of osmotic release methylphenidate (OROS-MPH), compared with placebo, in increasing the effectiveness of smoking cessation treatment (i.e., nicotine patch and counseling) and in ameliorating ADHD symptoms in smokers with ADHD.

**Methods:** This was a randomized, double-blind, placebo-controlled, 11-week trial. Two hundred and fifty five adults meeting DSM-IV criteria for ADHD and interested in quitting smoking were recruited across six sites and randomized to OROS-MPH (72 mg/day) or placebo. All participants received weekly individual smoking cessation counseling for 11 weeks and 21 mg/day nicotine patch starting on the smoking quit day (day 27) through study week 11. Efficacy measures included prolonged abstinence during study weeks 7-10, cigarettes per day, and the DSM-IV ADHD Rating Scale (ADHD-RS). Safety measures included vital signs and adverse events.

**Results:** Two hundred and fifteen participants (i.e., 84%) completed the 11-week active phase. Prolonged abstinence rates, 43.3% and 42.2%, for the OROS-MPH and placebo groups, respectively, did not differ significantly (p=0.81). OROS-MPH, relative to placebo, evidenced a greater reduction in DSM-IV ADHD-RS score (p<0.0001) and in cigarettes per day during the post-quit phase (p=.016). OROS-MPH, relative to placebo, increased blood pressure and heart rate to a statistically, but not clinically, significant degree; medication discontinuation did not differ significantly between treatments.

**Conclusions:** OROS-MPH, relative to placebo, did not improve smoking abstinence, effectively treated ADHD and was safe and generally well tolerated.

**Support:** National Institute on Drug Abuse, Center for Clinical Trials Network.

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# PROSPECTIVE STUDY OF ADHD AND RISK FOR DRUG ABUSE.

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**Aims:** To compare childhood-defined ADHD groups and matched controls on the extent and pattern of subsequent drug use behaviors, including substance use disorders, during late adolescence and young adulthood.

**Methods:** We present self-reported drug use behaviors from assessment waves 4 - 6 of ADHD probands (n = 125) and matched controls (n = 91) (ages 19 - 24) recruited from the community. Extent and pattern of drug use involvement, including substance use disorders, are compared between the a) ADHD and control groups, b) ADHD youth who vary with respect to the presence of externalizing disorders (ODD, CD), and c) ADHD youth with persistent ADHD symptoms versus non-persistent ADHD symptoms.

**Results:** The findings indicate consistent and significant (all p levels > .05) elevations on all drug use involvement and SUD measures for the ADHD + externalizing group when compared to the ADHD-only and controls. There were no significant differences on any of the drug outcome variables between the ADHD-only and control groups. Also, among youth that revealed a persistence of ADHD into young adulthood, drug use behaviors were significantly elevated (all p levels > .05) compared to ADHD youth whose symptoms desisted.

**Conclusions:** The presence of ADHD alone as a child does not appear to confer an elevated risk for drug use behaviors during late adolescence and young adulthood. However, ADHD youth that also reveal externalizing problems, such as ODD and CD), and those youth whose ADHD persisted into young adulthood, appear to be at elevated risk for subsequent drug use involvement and increased likelihood of a substance use disorder.

**Support:** This study was supported by grants K02 DA015347 and R01 DA012995 from the National Institute on Drug Abuse.

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# EFFECTS OF THE TETRAHYDROPROTOBERBERINES L-TETRAHYDROPALMATINE AND L-STEPHOLIDINE ON COCAINE SELF-ADMINISTRATION UNDER FIXED AND PROGRESSIVE RATIO SCHEDULES AND COCAINE DISCRIMINATION IN RATS.

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**Aims:** Tetrahydroprotoberberines (THPBs) are naturally occurring alkaloids found in plants contained in many traditional Chinese herbal preparations. The pharmacological profiles of several THPBs, most notably l-tetrahydropalmatine (l-THP), a non-selective antagonist at dopamine receptors and l-stepholidine (l-SPD), an antagonist at D2-like receptors and a partial agonist at D1 receptors, suggest that they may have utility as pharmacotherapeutic agents for the management of cocaine addiction. Accordingly, we and others have shown that l-THP attenuates cocaine reinforcement, cocaine-precipitated relapse, and cocaine-induced decreases in ICSS thresholds in rats at doses that do not produce non-specific response deficits and reduces craving and relapse in recovering heroin addicts.

**Methods:** To further examine the potential usefulness of THPBs for treating cocaine addiction, the effects of l-THP and l-SPD on cocaine self-administration (SA) under a progressive ratio (PR) schedule and on the discriminative stimulus effects of cocaine were determined in adult male Sprague-Dawley rats.

**Results:** l-THP (v, 1.8375, 3.75, 7.5 mg/kg, ip) dose-dependently reduced breaking points for cocaine (0.5, 1.0 mg/kg/inf) SA under a PR schedule and produced a rightward shift in the dose-response curve for cocaine discrimination in rats trained to discriminate cocaine from saline in a 2-lever FR20 sucrose pellet-reinforced procedure. Preliminary data indicate that, at similar doses, l-SPD has minimal effects on PR cocaine SA, presumably due to its short half-life combined with the long duration of the PR SA sessions. Effects of l-SPD on cocaine discrimination and FR SA during shorter sessions will be reported.

**Conclusions:** These findings suggest that l-THP, l-SPD, and other THPB compounds may represent new agents with potential usefulness for treating cocaine addiction.

**Support:** Supported by NIH Grant DA15758 to JRM

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# PHASE II, RANDOMIZED, DOUBLE-BLIND STUDY IN FASTED AND FED HEALTHY SUBJECTS TO EVALUATE THE DOSE-RESPONSE FOR FLUSHING, TOLERABILITY, AND SAFETY OF ESCALATING DOSES OF NIACIN.

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**Aims:** To evaluate the dose-response of niacin-induced flushing, the safety and tolerability of various niacin doses, and the food effect on niacin side effects in healthy subjects. ACUROX<sup>®</sup> Tablets contain oxycodone HCl and a small niacin dose (30 mg) to discourage excessive oral consumption.

**Methods:** 50 healthy subjects received 8 niacin doses (30, 60, 90, 120, 240, 360, 480 and 600 mg) and 3 placebo doses on 11 separate days in random order. Half of the subjects were dosed after an overnight fast; the other half ate a standard high-fat meal before dosing. Tolerability was assessed 3 hrs postdose using a Niacin Tolerability Rating Scale (TRS). Safety evaluations included vital sign, clinical laboratory, and adverse event (AE) assessments.

**Results:** A niacin tolerability dose-response relationship was observed in fasted subjects and at doses >240 mg in fed subjects. A significant food effect was noted in niacin TRS scores ( $P < 0.0001$ ) across all dose levels. 46% of fasted subjects rated the 240 mg dose as "mildly unpleasant, but tolerable," "unpleasant and difficult to tolerate," or "intolerable and would never take again." This percentage rose to 73%, 86% and 88% for 360, 480 and 600 mg niacin, respectively. In contrast, the percentages of fed subjects reporting "no effect" or "easy to tolerate" were 100%, 92%, 76% and 68% for 240, 360, 480 and 600 mg niacin, respectively. No serious AEs were reported. A dose-related trend for flushing and pruritis was noted in fasted subjects. At the 4 highest doses, flushing was reported by 54%-88% of subjects, and pruritis by 25%-43% of subjects. A dose-related trend for flushing was noted in fed subjects at doses  $\geq 240$ mg. No treatment-emergent safety issues were observed.

**Conclusions:** Niacin was well tolerated at 30 and 60 mg; side effects generally were dose-dependent across the dose range. Most fasted subjects reported undesirable side effects such as flushing at niacin doses  $\geq 240$ mg. Niacin side effects were mitigated by food.

**Support:** King Pharmaceuticals<sup>®</sup>, Inc.

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# COCAINE-SEEKING AFTER COCAINE SELF-ADMINISTRATION IS ASSOCIATED WITH PLASTICITY OF THE SEROTONIN 5-HT2C RECEPTOR IN THE PREFRONTAL CORTEX.

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**Aims:** The 5-HT2CR (5-HT2CR) in the prefrontal cortex (PFC) has been identified as an important mediator of the behavioral effects of psychostimulants such as cocaine. The purpose of this experiment was to determine the time-dependent neuroadaptive changes in the 5-HT2CR following periods of forced abstinence from chronic cocaine self-administration (SA).

**Methods:** Male Sprague-Dawley rats were trained to self-administer cocaine (active group, 0.75 mg/kg/0.1 ml i.v.) under a fixed ratio (FR) 5 schedule of reinforcement, while yoked animals passively received saline according to the active animal's pattern of administration, for a period of 15 days. Subsequently, the response to conditioned cues at 1 and 30 days of forced abstinence from cocaine self-administration was assessed (Western blot), along with the expression of the 5-HT2CR expression in PFC at 1 and 30 days.

**Results:** Preliminary results indicate that cocaine-seeking was significantly elevated on Day 1 of withdrawal ( $p < 0.05$ ) and further elevated by Day 30 ("incubation";  $p < 0.05$ ). Western blot analyses indicate that the expression of 5-HT2CR protein levels in the prefrontal cortex of the cocaine group were significantly elevated on Day 1 ( $p < 0.05$ ) and reduced below baseline at Day 30 of withdrawal ( $p < 0.05$ ) as compared to the corresponding yoked saline group. A significant correlation was observed such that higher 5-HT2CR expression in the PFC is associated with lower cocaine-seeking.

**Conclusions:** The 5-HT2CR in the PFC is dynamically responsive to cocaine exposure and/or abstinence. Neuroadaptations of the 5-HT2CR may impact inhibitory output of the PFC and contribute to cue-evoked activation in the PFC of cocaine addicts. 5-HT2CR signaling in the PFC may provide a therapeutic target for the prevention of relapse to drug use.

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# EFFECTS OF ORAL VS. INTRAPERITONEAL METHYLPHENIDATE ON LOCOMOTOR ACTIVITY AND CONDITIONED PLACE PREFERENCE IN RATS.

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**Aims:** Methylphenidate (MPH) is a stimulant drug used to treat attention-deficit/hyperactivity disorder (ADHD). Most ADHD patients do not abuse oral (PO) MPH, yet evidence suggests that MPH tablets are often diverted to be crushed and insufflated for abuse purposes, perhaps due to the more rapid brain uptake and greater bioavailability provided by this latter route. The present work compared the effects of PO and intraperitoneal (IP) MPH on locomotor activity and conditioned place preference (CPP) in rats.

**Methods:** In two different experiments, adult male Sprague-Dawley rats ( $n=16$  per experiment) were first trained to consume saline (SAL)-filled crackers and then were assigned randomly to 1 of 3 different drug treatment groups: Group 1 received PO SAL, followed immediately by IP SAL; Group 2 received PO SAL followed by IP MPH; and Group 3 received PO MPH followed by IP SAL ( $n=4-6$  per group). The dose of MPH with each route was 10 mg/kg. In Experiment 1, locomotor activity was monitored for 1 hr immediately following drug treatment for 10 consecutive days. After a 21-day drug-free period, rats were challenged across 3 consecutive daily locomotor tests with the following treatments: PO SAL / IP SAL; PO SAL / IP MPH; and PO MPH / IP SAL. In Experiment 2, each of the different drug treatments were paired on 4 trials with one side (counterbalanced) of a 3-compartment CPP apparatus for 30 min; the other side was paired with SAL on 4 30-min trials. Rats then received PO SAL / IP SAL immediately prior to a 15-min CPP post-test.

**Results:** In Experiment 1, IP MPH produced acute hyperactivity, sensitization and conditioned hyperactivity; however, PO MPH had no reliable effects. In Experiment 2, both PO and IP MPH produced CPP.

**Conclusions:** The locomotor effects of IP MPH are greater than those of PO MPH. However, IP and PO MPH-treated rats displayed similar CPP, suggesting that MPH may have abuse liability with either route.

**Support:** Supported by USPHS grants DA 05312 and DA 023853.



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### PROBLEM SEVERITY AND TREATMENT NEEDS AMONG NATIVE AMERICAN/ALASKA NATIVE AND ASIAN AMERICAN/PACIFIC ISLANDER DRUG ABUSERS.

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**Aims:** This study investigates patterns of drug use and other related treatment needs among Native American/Alaska Native (NA/AN) and Asian American/Pacific Islander (AAPI) drug abusers.

**Methods:** Based on two data sources (Methamphetamine Treatment Follow-Up Study & Treatment System Impact and Outcomes of Proposition 36), 301 AAPIs and 276 NA/ANs were identified. These subjects were then compared with other ethnic groups, including 4263 Caucasians, 1062 African Americans, and 1948 Hispanics, in the same data sources. Addiction Severity Index (ASI) was administered at both intake and the 12-month follow-up.

**Results:** 1) The overall analysis of variance was significant for all seven aspects of ASI. 2) Post hoc tests show that the NA/AN group, together with African Americans, had the highest alcohol use at baseline compared with the other groups. 3) In terms of drug use, the AAPIs and NA/ANs had higher severity scores than their African American and Hispanic counterparts, but more on the same level with the Caucasian group. 4) While the NA/AN group demonstrated greater problem severity and thus greater needs in employment, the AAPIs had the least problem with employment at intake. 5) AAPI drug users indicated the greatest needs in dealing with family issues. 6) Legal problems were as severe for AAPIs and NA/ANs as for Caucasians and Hispanics. The African American group had the highest problem severity in the legal domain. 7) While AAPIs were in the best health conditions at intake, the NA/AN group showed significantly higher medical needs than any other group. 8) NA/AN drug users also demonstrated greater psychological needs than other groups.

**Conclusions:** These results, as well as other measures collected by the study, identified areas that need special attention in treating NA/AN and AAPI drug users in order to adequately address their specific needs and to optimize their treatment outcomes.

**Support:** This study is funded by a NIDA diversity supplement to Grant # P30 DA016383 (PI: Hser) & K05DA017648 (Hser).

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### DEPRESSED COCAINE-DEPENDENT AND CANNABIS-DEPENDENT INDIVIDUALS SEEKING TREATMENT: COMPARISON OF PSYCHIATRIC SYMPTOMATOLOGY.

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**Aims:** The two most commonly abused illicit drugs in the United States are marijuana and cocaine. Comorbid depression is also common in these substance-abusing populations. Our study compared symptoms of 1) depression and 2) substance use dependence in treatment seeking individuals with major depression and cocaine dependence (COC) and major depression and cannabis dependence (MJ).

**Methods:** Depression and dependence symptoms were determined by the SCID for DSM-IV. The total sample consisted of 75 participants (38 ± 11 yrs) who were predominately male (78%) and 37% black, 28% white, 28% Hispanic, and 7% other. There were no significant demographic differences between the two groups.

**Results:** Comparisons of depression symptoms revealed no significant differences in the total number of symptoms between the two groups. Comparisons of dependence symptoms, revealed a trend with the COC group endorsing a greater number of total symptoms than the MJ group (6.3+1 vs 5.6+1.2;  $t = -2.5$ ,  $p = .06$ ). In regards to specific dependence symptoms, the COC group was significantly more likely to endorse symptoms of "using more than intends to" ( $\chi^2=5.9$ ,  $p = .02$ ), "dysphoric mood due to use" ( $\chi^2=6.9$ ,  $p < .01$ ) and "feel withdrawal effects" ( $\chi^2=4.3$ ,  $p < .05$ ) than the MJ group. Exploring the relationship between depressive and dependence symptoms, we found that the total number of depression symptoms was positively correlated with the total number of dependence symptoms in the COC group ( $r = .39$ ,  $p < .05$ ); however, this was not true in the MJ group.

**Conclusions:** Our analyses indicate that there are differences between depressed cocaine and depressed marijuana users in terms of their depressive and dependence symptomatology. Identifying these differences may aid in developing targeted interventions specific for these unique populations.

**Support:** NIDA # RO1DA022217 & P50DA09236

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### MEDICAL EXAMINER METHADONE-RELATED DRUG DEATHS: SINGLE VS POLYDRUG ABUSE.

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**Aims:** US poisoning deaths involving methadone have increased nearly 5-fold over the last decade. The purpose of this study was to characterize fatal methadone poisonings between 1997 and 2003 from the Office of Chief Medical Examiner, Western District, Virginia.

**Methods:** Medical examiner deaths were reviewed to identify methadone related drug deaths. Autopsy reports, physician notes, pharmacy logs, death investigations, and toxicology results were reviewed.

**Results:** Methadone-related deaths increased from 5 to 85 cases from 1997 to 2003 in western Virginia. Methadone was the most common opioid identified on toxicology in 249 (28%) of the 889 total drug deaths. Of the 249 cases, 62 were female (mean age 38.1 years) and 187 were male (mean age 36.9 years). The manner of death was predominantly accidental (87%) rather than suicide (10%) or undetermined or natural (3%). The cause of death was polydrug toxicity in 224 (90%) of the cases, while 25 cases (10%) had only methadone. The decedent had been prescribed methadone in only 24% of the 249 cases. The mean blood methadone concentration was 0.495 mg/L in the polydrug overdose deaths and 0.518 mg/L in the 25 cases where methadone was found singularly. In the polydrug overdose cohort, the most common co-occurring toxicology findings were diazepam (32.9% of cases), sertraline (26%), venlafaxine (24%), ethanol (22%), alprazolam (19%), hydrocodone (13.3%), cocaine (10%), and oxycodone (10%).

**Conclusions:** Methadone-related deaths increased precipitously in rural western Virginia over the 7-year study period consistent with national trends. Methadone was the penultimate opioid identified in all drug-related deaths. Post-mortem blood methadone concentrations did not differentiate methadone-only and polydrug cases. While concentrations were within the therapeutic range for methadone maintenance, opioid tolerance among decedents was unknown. Most decedents combined it with other drugs and procured methadone illicitly.

**Support:** RO3DA019047

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### A RECEPTOR MECHANISM FOR METHAMPHETAMINE ACTION IN DOPAMINE TRANSPORTER REGULATION.

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**Aims:** Methamphetamine, a highly addictive psychostimulant drug, is a substrate for the dopamine transporter (DAT) and interferes with dopamine (DA) transport via competitive and non-competitive cascades. We and others previously reported that trace amine-associated receptor 1 (TAAR1) is expressed in dopaminergic nuclei and is activated by methamphetamine *in vitro*. This study is to investigate whether and how TAAR1 is implicated in methamphetamine action.

**Methods:** We used transfected cells and brain striatal synaptosomes to investigate roles of TAAR1 in [3H]dopamine uptake and efflux and in DAT trafficking at exposure to methamphetamine.

**Results:** We found that TAAR1 activation by methamphetamine dramatically inhibited [3H]dopamine uptake in transfected cells and in monkey and mouse striatal synaptosomes by comparing methamphetamine effects in cells with/without TAAR1 expression or in the striatal synaptosomes of wild type and TAAR1 knockout mice. We also found that TAAR1 regulates [3H]dopamine efflux in response to methamphetamine. When cells or synaptosomes were loaded with a low concentration (10 nM) of [3H]dopamine, methamphetamine caused [3H]dopamine efflux in a TAAR1-dependent manner, whereas when cells or synaptosomes were loaded with a high concentration (1  $\mu$ M) of [3H]dopamine, methamphetamine induced more [3H]dopamine efflux in the presence of TAAR1. Furthermore, we found that methamphetamine reduced DAT level on the surface membrane in the presence but not in the absence of TAAR1, suggesting that methamphetamine-caused DAT trafficking is associated with TAAR1 activity. Finally, we demonstrated that all TAAR1-mediated effects in methamphetamine action were associated with PKA- or PKC-dependent phosphorylation cascades, suggesting that TAAR1 may play determinant roles in methamphetamine-elicited phosphorylation events.

**Conclusions:** Taken together, this study reveals a receptor mechanism for methamphetamine action in DAT regulation and may reveal a potential therapeutic target for methamphetamine addiction.

**Support:** Support by NIH grants DA022323 (GMM) and DA016606 (GMM)

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### CM156, A NOVEL ANTAGONIST OF $\sigma$ RECEPTORS, ATTENUATES COCAINE-INDUCED CONDITIONED PLACE PREFERENCE: BEHAVIORAL EVALUATIONS AND MOLECULAR ANALYSIS.

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**Aims:** This study investigates the potential role of  $\sigma$  receptors in cocaine-induced conditioned place preference (CPP).

**Methods:** CM156, a novel antagonist with high selectivity and affinity for  $\sigma$  receptors, was evaluated in CPP studies. Male, Swiss Webster mice were assigned to the following groups: saline/saline, saline/cocaine (20 mg/kg, i.p.), CM156 (1, 10 or 20 mg/kg, i.p.)/cocaine or CM156/saline. After CPP behavioral evaluations, mouse brain tissues were collected. Alterations of gene expression in half brain samples in different groups were screened by cDNA microarray analysis. Genes with significant changes in expression were further confirmed by quantitative real-time PCR. Protein expression of the genes of interest is being confirmed by Western blotting.

**Results:** In behavioral evaluations, CM156 blocked the expression of CPP. Four genes exhibited significant changes in the microarray analysis including metastasis associated lung adenocarcinoma transcript 1 (malat1), splicing factor, arginine/serine-rich 18 (sfrs18), tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein (yw haz) and transthyretin (ttr). Three genes were confirmed by quantitative real-time PCR including malat1, yw haz and ttr. The protein expression of Ttr is being evaluated by Western blotting.

**Conclusions:** CM156, an antagonist of  $\sigma$  receptors, attenuates the expression of CPP, which suggests  $\sigma$  receptors play critical roles in CPP. The mechanisms of action of  $\sigma$  receptors in CPP appear to involve interactions with Malat1, Yw haz, Sfrs18 and Ttr.

**Support:** DA011979

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### TEMPORAL DISCOUNTING AND PROCRASTINATION AS PREDICTORS IN A LABORATORY MODEL OF SMOKING ABSTINENCE.

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**Aims:** The specific aim of this study is to demonstrate the predictability to abstain from smoking during an abstinence test.

**Methods:** Forty cigarette smokers completed 2 sessions of a smoking abstinence test. In each 3-hour session, each consecutive 5-minute interval of maintained abstinence resulted in a virtual fishbowl draw modeled on Petry's method. Smoking during the abstinence test resulted in a continuation of the session with no further opportunity to earn draws.

**Results:** Fourteen of 40 participants smoked in at least 1 session, while the remaining 26 did not smoke in either session. Demographic, temporal discounting, procrastination, and locus-of-control measures collected prior to abstinence tests were examined as possible predictors of smoking during a session. Demographic variables and locus-of-control measures did not differentiate between participants who did and did not smoke. In contrast, temporal discounting for \$50 of future hypothetical money did differentiate these groups ( $p < .05$ ), with those who smoked discounting more than those who did not. Additionally, two different procrastination scales (Procrastination Scale and TPS 16) revealed nearly significant differences between smokers who did and did not smoke ( $p = .09$ ), with more procrastination observed in those who did smoke during the abstinence test.

**Conclusions:** These results indicate that both temporal discounting and procrastination, both of which assess some form of intertemporal decision-making, may be factors relevant in efforts to maintain smoking abstinence by smokers.

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### SUGAR DEPENDENCE IN LOW- VS. HIGH-SACCHARIN CONSUMING RATS.

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**Aims:** Intermittent glucose access can produce opioid-mediated dependence in rats. This effect was examined in rats selectively bred for high (HiS) and low (LoS) saccharin intake. LoS rats self-administer less cocaine or ethanol but show more ethanol withdrawal and food-deprivation-induced hyperactivity (Carroll et al., 2008).

**Methods:** Procedures replicated Colantuoni et al. (2002), who reported spontaneous withdrawal after 8 days of glucose access. Adult rats (32 in each line) were fed 12 h daily; half got 25% glucose during feeding. On Day 15 (24 h abstinent), motor signs of withdrawal and acoustic startle (30 95-dB trials 10 s apart) were measured. Naloxone (20 mg/kg ip) was given to half of each group before testing. Groups were compared with analyses of variance. The correlation between glucose intake and startle in each line also was assessed.

**Results:** Glucose intake was positively correlated with startle in LoS rats but not in HiS rats. Normally, sweet intake is inversely related to startle (Dess et al. 2000). Thus, this correlation likely reflects vulnerability to sugar dependence which is expressed only among LoS rats who drink glucose to excess. Regardless of glucose access, tremors and jaw movements were frequent, and naloxone enhanced the latter; naloxone also reduced startle in HiS rats but had no effect on LoS rats.

**Conclusions:** These findings suggest greater sugar dependence in LoS rats and a larger effect of 12-h feeding on endogenous opioids in HiS rats. In a second study, food-deprived and freely fed rats (24 per line) were tested on a hotplate on Days 5 and 17. Half received naloxone (3 mg/kg ip) before a retest on Day 17. ANOVAs on pawlick latencies on Day 5 and on the Day 17 retest showed that deprivation increased latencies in both lines. Trends toward naloxone reversal and a larger effect in HiS rats were observed. Work continues on effects of deprivation on opioid function in LoS and HiS rats, its relevance to vulnerability to withdrawal and drug-seeking, and implications for risk of drug dependence and comorbid eating disorders in humans.

**Support:** Supported by a Fletcher Jones Foundation grant to Occidental College

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### PREDICTORS OF INITIAL ABSTINENCE IN NEWLY PREGNANT WOMEN.

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**Aims:** Maternal smoking is a leading preventable cause of poor pregnancy outcomes and infant morbidity and mortality. Despite the existence of effective interventions, end-of-pregnancy rates are often low (<20%). Greater knowledge of factors influencing smoking cessation during pregnancy is therefore needed to understand smoking in this population and to develop more effective interventions.

**Methods:** Participants (N = 131) were involved in two separate clinical trials examining the use of incentives in either promoting or maintaining smoking abstinence during pregnancy and up to 6-mo postpartum. One group of women was still smoking at intake (start of prenatal care), whereas the other group had quit smoking prior to intake once they discovered that they were pregnant. Our group was in a position to identify potential variables associated with smoking status among these women. Socio-demographic, smoking characteristics, and history of depressive symptoms were assessed. Additionally, delay-discounting (DD) task for hypothetical monetary rewards was assessed to examine the influence of temporal horizons on smoking status.

**Results:** DD was significantly greater in women who continued to smoke relative to those who had stopped once they were pregnant in univariate analyses, but not in multivariate analyses. Instead, in multivariate analyses, women who were still smoking and those that had stopped were differentiated by education level, age of first cigarette, working outside of the home, and smoking availability (other smokers in the house) and severity (# cigs/day smoked pre-pregnancy).

**Conclusions:** These results suggest that women who quit smoking discount the future less than those who continue smoking, but that difference does not appear to account for unique variance in smoking status upon entering prenatal care.

**Support:** This research was supported in part by National Institute on Drug Abuse Research Grant DA 14028 and Training Grant DA 007242.

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### ROLE OF THE DOPAMINE RECEPTOR SUBTYPES IN THE EXPRESSION OF THE DISCRIMINATIVE STIMULUS EFFECT INDUCED BY U-50,488H OR METHAMPHETAMINE.

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**Aims:** Kappa-opioid receptor agonist, such as U-50,488H, produced the aversive effects. Based on several studies, activation of the mesolimbic dopamine system is thought to be responsible for the drug-induced either rewarding or aversive effects. Therefore, the present study was designed to ascertain the role of the dopamine receptor subtypes in the discriminative stimulus effect induced by either U-50,488H (3 mg/kg, i.p.) or methamphetamine (METH; 1 mg/kg, i.p.). **Methods:** Fischer 344 rats were trained to discriminate between drugs and saline under a fixed-ratio 10 food-reinforced procedure.

**Results:** The dopamine D1 receptor antagonist SCH 23390 produced a partial generalization to the discriminative stimulus effect induced by U-50,488H (67% of U-50,488H-lever responding). In contrast, the D2 receptor antagonist sulpiride substituted for U-50,488H cue (>80% of U-50,488H-lever responding). The D2 receptor agonist (R)-propylnorapomorphine (NPA) failed to substitute for U-50,488H cue (36% of U-50,488H-lever responding), while the D3 receptor-preferred agonist 7-OH-DPAT at low doses completely substituted for U-50,488H cue. However, higher doses of 7-OH-DPAT produced a gradual decline in the U-50,488H-lever responding. Furthermore, NPA and 7-OH-DPAT at high doses substituted for the discriminative stimulus effect induced by METH (>80% of METH-lever responding) in a dose-dependent manner, indicating that 7-OH-DPAT at high doses may interact with D2 receptors.

**Conclusions:** These findings suggest that the blockade of D2 receptor may be critical for the production of the discriminative stimulus effect induced by U-50,488H, whereas the stimulation of D2 receptor may contribute to the production of the discriminative stimulus effect induced by METH. Furthermore, D3 receptor may play a role of the negative regulatory effects in the dopaminergic neurotransmission.

**Support:** Grants from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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### SOCIAL AND ENVIRONMENTAL FACTORS ALTER THE EFFECTS OF MDMA ON ACTIVITY AND COCAINE CONDITIONED PLACE PREFERENCE IN ADOLESCENT RATS.

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**Aims:** MDMA (ecstasy) is used predominately by adolescents and young adults and young MDMA users are more likely to use other drugs, including cocaine, compared to non- MDMA users. Studies have shown that 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 environmental conditions alter the effects of MDMA on locomotor activity and cocaine conditioned place preference (CPP).

**Methods:** Male rats were housed on PND 23 in either an impoverished (II, singly housed with no toys) or enriched (SE3, 3 rats/cage with toys) condition. Beginning on PND 32, rats were pretreated daily with 2 mg/kg MDMA for five days and locomotor activity was recorded on days 1,2 and 5. Starting at PND 37, cocaine CPP was done to see if the effect of prior treatment with MDMA on subsequent cocaine conditioned reward was altered by the housing conditions.

**Results:** Saline-pretreated SE3 rats showed significantly lower activity levels compared to II rats. This dose of MDMA had little effect on locomotor activity regardless of housing, compared to saline-pretreatment. There were no differences in the development of cocaine CPP in the II and SE3 saline-pretreated groups. In addition, there were no differences between saline and MDMA pretreatment in the development of CPP in II rats. However, in SE3 rats, there was an increase in the magnitude of the CPP after pretreatment with MDMA compared to saline.

**Conclusions:** Pretreatment with MDMA differentially affected cocaine CPP in enriched vs impoverished rats. Further studies will need to be done to determine what roles the social or the environmental enrichment play in mediating these differences.

**Support:** NIDA and ORWH grants DA024584 and DA015119

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### DIFFERENCE IN ALLELIC FREQUENCY IN TWO ETHNIC GROUPS AND ANALYSIS OF POSSIBLE ASSOCIATION OF THE 830 BP INDEL POLYMORPHISM IN THE OPRK1 PROMOTER WITH COCAINE AND/OR ALCOHOL DEPENDENCE.

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**Aims:** A number of single nucleotide polymorphisms and haplotypes of the human kappa opioid receptor gene, OPRK1, have been reported to be associated with vulnerability to develop specific drug and alcohol addictions. Recently, the presence of an 830 bp insertion (a functional indel) in the OPRK1 promoter was found to be associated with alcohol dependence in Caucasians (Edenberg et al, 2008). We tested this OPRK1 indel polymorphism for possible association with cocaine dependence and cocaine/alcohol codependence.

**Methods:** We applied a PCR assay and gel electrophoresis analysis to genotype the OPRK1 830 bp indel in 187 African Americans (74 controls and 113 cocaine dependent or cocaine/alcohol codependent) and 108 Caucasians (64 and 44, respectively).

**Results:** There was no significant deviation of genotype distributions from Hardy-Weinberg equilibrium in control and case subjects. There was a significant difference in the frequency of the insertion between two ethnic groups in the control subjects, with higher allele frequency in African Americans (0.66) than in Caucasians (0.44) (p=0.0002). There were no significant differences in the insertion or deletion allele or genotype frequency distributions between cases and controls in either ethnic group.

**Conclusions:** Further analysis of linkage disequilibrium of the 830 bp indel with other OPRK1 polymorphisms will provide more information on a potential role of this indel in the development of cocaine dependence.

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### CESSATION TREATMENT FOR SMOKERS WITH SERIOUS MENTAL ILLNESS.

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**Aims:** Individuals with serious mental illness (SMI), such as schizophrenia and bipolar disorder are 2 to 3 times more likely to smoke than the general population, report heavier smoking and greater levels of tobacco dependence, and seem to find it more difficult to quit smoking. The objective of this study was to identify the factors associated with successful smoking cessation among SMI patients in a specialized clinic setting.

**Methods:** We conducted a retrospective chart review of patients with concurrent SMI and healthy controls who sought treatment for tobacco dependence at the Nicotine Dependence Clinic at the Centre for Addiction and Mental Health in Toronto, Canada from 2002-2006. Patients with SMI (n=39) were age and sex matched with controls (n=78) (1:2 ratio).

**Results:** At baseline SMI patients were heavier smokers (32.9 vs. 22.4 cpd; p<0.01), and were more nicotine dependent by FTND scores (7.1 vs. 6.2; p<0.06). During treatment, SMI patients received higher doses of nicotine replacement therapy (32 mg vs 24 mg; p<0.01), were more likely to supplement patch use with nicotine gum (89% vs. 70%; p<0.05), and made more visits to the clinic (14.1 vs 8.9; p<0.05). At the end of treatment, quit rates were higher among SMI patients than controls (45% vs. 24%; p<0.05). Predictors of quitting among SMI patients included the number of clinic visits and their motivation for quitting at baseline. Further analysis of this dataset will be presented.

**Conclusions:** These findings suggest that with sufficient behavioural and pharmacological support patients with SMI quit smoking at similar rates to healthy controls.

**Support:** This study was funded by the Ontario Tobacco Research Unit.

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**EFFECT OF MIXED DRUG USE ON HIV SEROSTATUS AND LIFE FUNCTIONING IN UKRAINIAN INJECTION DRUG USERS.**

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**Aims:** Previous research indicated that mixing opiates with other substances may increase HIV risk among injection drug users (IDU) in Ukraine. The aims of this study are to confirm this mechanism of influence and assess actual prevalence of HIV among those who mix drugs.

**Methods:** This is an analysis of baseline data from a clinical trial of behavioral treatment efficacy. The sample was recruited from IDUs entering treatment in Vinnitsya, Ukraine. Measurements included rapid HIV testing, Addiction Severity Index (ASI), Blood Borne Virus Transmission Risk Assessment Questionnaire (BBV-TRAQ), and Brief Symptom Inventory (BSI).

**Results:** The main drug of abuse in Ukraine is home-made opiate solution. Other substances are added to heighten effects, minimize side effects, and clarify it. Of 121 people with past-month opiate use, 58.9% mixed with dimedrol (DI); 17.7% with benzodiazepines (BD); 37.8% with hypnotics (HY). 30-day frequency of mixing with BD or with HY correlated positively with HIV risk behavior score (BBV-TRAQ) (BD Spearman's  $r=0.19$ ,  $p<0.064$ ; and HY  $r=0.28$ ,  $p=0.004$ ). In a logistical model controlling for risky behaviors, age and gender, lifetime mixing with HY was a positive predictor of HIV status (aOR=2.9,  $p=0.046$ ). Lifetime history of mixing with BD correlated with higher ASI medical problem score ( $p<0.001$ ), and BSI psychological distress ( $p=.02$ ). 30-day opiate mixing with DI, BD, and HY was associated with higher ASI severity of drug use (DI  $p=0.04$ , BD  $p=0.02$ , HY  $p=0.0001$ ), largely due to increased other drug use (amphetamines, cannabis, hallucinogens).

**Conclusions:** Mixing opiates with HY is associated with HIV-positive serostatus. This effect is not mediated by behavioral variables and should be a topic of further research. Mixing opiates with DI, HY, and BD also correlates with severity of addiction and health outcomes.

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**CHARACTERISTICS OF HEROIN USERS IN METHADONE MAINTENANCE TREATMENT CLINICS IN WUHAN, CHINA.**

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**Aims:** To curtail the spread of drug use and related problems, including HIV or other blood borne and infectious diseases, 20 methadone maintenance treatment (MMT) clinics will have opened in Wuhan, China by the end of 2008 and are operating under the umbrella of the Wuhan Center for Disease Control and Prevention. This study is to determine the characteristics of the heroin users in the MMT clinics in Wuhan city.

**Methods:** Socio-demographic and risk data from heroin dependent individuals undergoing MMT were collected at entry to MMT. Additionally, blood samples were collected and tested for HIV and HCV at entry, 6 and 12 months after MMT enrollment.

**Results:** A total of 3074 individuals enrolled in 16 MMT clinics in Wuhan between Jan 2007 and Oct 2008 were investigated. 71.6% of them were male, 28.4% female, 61.1% were younger than 40 years, and 57.5% were unmarried at admission; 65.6% had middle school level education, 88.2% did not have a stable job, and 59.0% depended on family or friends for living costs during the past six months; 66.2% were below 30 years old when they first began abusing drugs, 74.7% injected heroin during the six months prior to MMT entry, and 83.8% reported lifetime history of sharing needles; 30.6% had more than two sex partners in the past six months, and 82.1% had recent sex without condoms. At MMT entry, 1.1% were HIV positive and 75.2% HCV positive; 6 of the 3074 participants acquired HIV within 6 months after MMT enrollment.

**Conclusions:** Heroin users entering MMT in Wuhan are at very high transmission risk for blood borne infections, as indicated by the high rates of IDU, needle sharing, sexual activity, and unprotected sexual activity. The relatively low seroconversion during MMT reflects both the reductions in risk associated with MMT and the low current prevalence of HIV among IDUs, but the population of untreated heroin users in Wuhan is still at great risk for an explosive HIV epidemic as a result of sexual transmission.

**Support:** 3 R01 DA014718-05A1S1

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**DEVELOPMENT OF BIARYL UREA ANALOGS OF SB-334867 AS OREXIN-1 RECEPTOR ANTAGONISTS.**

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**Aims:** Orexins are endogenous peptides that interact with two orexin receptors (OX1, OX2). Modulation of orexin receptors has been implicated in a number of physiological functions, including energy metabolism, control of feeding, neuroendocrine function, and regulation of arousal and the sleep-wake cycle. SB-334867, a potent and highly selective orexin-1 receptor antagonist, is active in vivo yet it suffers from poor aqueous solubility and low bioavailability (10%). Moreover, limited structure-activity information is available to guide future ligand design. In order to successfully develop novel structures having improved drug-like properties, a better understanding of the basic structure-activity relationships of SB-334867 is required.

**Methods:** Synthesized compounds were fully characterized using <sup>1</sup>H and <sup>13</sup>C NMR, Mass Spectrometry and HPLC. A calcium-dependent functional assay was employed to evaluate target compounds using a FlexStation II 384 and the calcium-4 dye kit in RD-HGA16 (Molecular Devices) cell lines stably expressing the OX1 receptor.

**Results:** In the calcium functional assay, SB-334867 showed good activity ( $K_e = 50$  nM), in agreement with reported values from radioligand binding assays. Replacement of the naphthyridine with 2-methylquinoline led to a slight decrease in activity ( $K_e = 440$  nM). The more aqueous soluble 4-dialkylaminophenyl analogs seemed to completely retain activity when compared to the 2-methylbenzoxazole-6-yl group. Unsubstituted, monosubstituted or acylated 4-aminophenyl analogs all resulted in the complete loss of activity.

**Conclusions:** We have developed a series of analogs of SB-334867 and characterized them using a calcium mobilization functional assay. Some of the compounds showed comparable potency to SB-334867 and should be of value in developing more drug-like ligands targeting the orexin-1 receptor.

**Support:** This research was funded by Research Triangle Institute.

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**BASAL AND COCAINE-INDUCED SEX DIFFERENCES IN THE DARPP-32 PATHWAY.**

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**Aims:** Behavioral and dopamine responses to cocaine are sexually dimorphic: female rats exhibit higher levels of locomotor and reward-associated behaviors after cocaine administration and dopamine release than do males. Activation of the DARPP-32 (dopamine- and cAMP-regulated phosphoprotein of Mr 32 kDa) intracellular cascade mediates responses to cocaine. It is yet to be determined if acute cocaine administration alters the DARPP-32 cascade in a sexually dimorphic pattern.

**Methods:** To address this issue, male and female rats received either saline or cocaine (30 mg/kg). Protein levels of DARPP-32, P-Thr34-DARPP-32 (phosphorylation of DARPP-32 at the Thr34 site), PP-1 (protein phosphatase 1), and PP-2B (protein phosphatase 2B) in the nucleus accumbens (NAc) were measured via Western blot analysis.

**Results:** Females had higher protein levels of DARPP-32, P-Thr34-DARPP-32, CaN-A (calcineurin A, catalytic subunit of PP-2B) and CaN-B (calcineurin B, regulatory subunit of PP-2B) than did males 5 min after saline treatment. CaN-A protein levels were also higher in females 15 min after saline administration. PP-1 protein levels were higher in females 30 min after saline treatment. Within each sex, no statistically significant differences were observed after saline administration. In male rats, cocaine treatment significantly increased CaN-A protein levels at 30 min and CaN-B protein levels at 15 min. In females, protein levels of DARPP-32, P-Thr34-DARPP-32 and CaN-A were significantly decreased 45 min after cocaine administration. However, cocaine treatment significantly elevated PP-1 protein levels at 30 min.

**Conclusions:** These novel results show that basal and cocaine-induced sex differences in the DARPP-32/ PP-1 cascade may be responsible for the sexual dimorphism in acute cocaine-induced behavioral responses.

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### LONG-TERM ALTERATIONS OF STRESS RESPONSIVE AND OPIOID SYSTEMS IN RAT HYPOTHALAMUS AND AMYGDALA DURING CHRONIC HEROIN WITHDRAWAL.

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**Aims:** We examined the effects of chronic heroin exposure and withdrawal on the HPA and HPG axes in response to acute heroin challenge in the rat.

**Methods:** In two separate studies, rats received chronic 10-day intermittent escalating-dose heroin administration (CIEHA) from 3x2.5 mg/kg/day on day 1 up to 3x20 mg/kg/day on day 10. In Study I, rats received a heroin challenge at 20 mg/kg or saline in the morning on day 11, after 12-h acute spontaneous withdrawal. In Study II, rats received a heroin challenge at 5 mg/kg or saline on day 21, following 10-d withdrawal from CIEHA. Plasma ACTH, corticosterone, LH and testosterone levels were measured 30 min after acute heroin challenge. Changes in mRNA expression of opioid genes (POMC, MOP-r and Dyn) and several stress responsive genes (CRF, CRF-R1 receptor, AVP, V1b receptor and orexin) were quantitatively measured in the hypothalamus, amygdala and pituitary.

**Results:** In Study I, we confirmed that both plasma ACTH and corticosterone levels were elevated after acute withdrawal. This HPA activation was attenuated 30 min after heroin challenge (20 mg/kg). In Study II, following 10-d withdrawal, HPA hormonal levels returned to baseline and acute heroin challenge at 5 mg/kg stimulated HPA activity in heroin naïve rats, but decreased ACTH levels in CIEHA-treated rats. Plasma LH levels were decreased by heroin challenge at 5 mg/kg following 10-d withdrawal, which was not found in heroin naïve rats. POMC mRNA levels in the medial hypothalamus were decreased following CIEHA and during acute withdrawal. In contrast, there was a rebound increase in the POMC mRNA levels after 10-d withdrawal. In the amygdala, AVP mRNA levels were increased after acute withdrawal and remained at higher than normal levels after 10-d withdrawal.

**Conclusions:** Our data suggest that (1) enhanced POMC gene expression after 10-d withdrawal is associated with inhibitory effects on HPA and HPG axes of acute heroin challenge; and (2) long-lasting alteration of amygdalar AVP gene expression may contribute to drug relapse after 10-d withdrawal.

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### CHARACTERIZATION OF ADOLESCENT PRESCRIPTION DRUG ABUSE AS REPORTED IN RADARS SYSTEM POISON CENTER DATA.

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**Aims:** Aims: For 2005, National Survey on Drug Use and Health (NSDUH) reported that 8% of adolescents misused a medication, and 3% endorsed substance use disorder symptoms related to prescription medication misuse. Using RADARS System Poison Center (PC) data, we assessed differences in outcomes and demographics between adolescent prescription opioid and stimulant intentional exposures.

**Methods:** Methods: PC use a standard electronic system to record spontaneous calls from the public and health professionals. RADARS System PCs (48 of 60 US PCs) perform quality control checks to verify coding accuracy. Intentional exposures in standardized categories (suspected suicide, misuse, abuse, unknown, withdrawal) are used as abuse and misuse surrogates. Adolescent (13-19yrs) intentional exposures involving opioids (buprenorphine, fentanyl, hydromorphone, hydrocodone, methadone, morphine, oxycodone, tramadol) or stimulants (methylphenidate, amphetamine) were analyzed (7/2007-6/2008). Known associated outcomes are defined as no effect, minor, moderate, major and death.

**Results:** Results: Of 2985 intentional exposures, 65% involved opioids. A greater proportion of opioid intentional exposures (n=131, 6.8%) were associated with major effects than stimulants (n=32, 3.0%). In addition, a greater proportion of opioid intentional exposures (n=5, 0.3%) were associated with death compared to stimulants (n=0, 0%). Mean age was 16.8 years for opioids and 16.0 years for stimulants (p<0.01). Similar results for associated outcome and age were obtained when abuse exposures were analyzed alone.

**Conclusions:** Conclusions: Significant differences in associated outcomes were found; of particular interest, no deaths were associated with stimulant intentional exposures. Significant differences for mean age and gender may inform development of effective interventions for adolescents.

**Support:** Support: Denver Health is a public non-profit organization providing data to industry, regulatory agencies and researchers through the RADARS System.

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### THE USE OF APPETITE SUPPRESSANT AMONG HEALTH SCIENCES UNDERGRADUATE STUDENTS IN SOUTHERN BRAZIL.

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**Aims:** Aim: To investigate the prevalence of appetite suppressant use among health sciences students in Southern Brazil.

**Methods:** Sample: 300 undergraduate students from seven courses of the University of Caxias do Sul, Brazil. Procedures: A cross-sectional survey was undertaken in which research participants completed a 24-question questionnaire.

**Results:** In this sample, 24.7% (n=74) were male and 75.3% (n=226) were female participants. The mean age was 28 (17-45). The sample was distributed according to undergraduate courses as follows: Biology 8% (n=24); Medicine 8.3% (n=25); Physiotherapy 14% (n=42), Nutrition 14% (n=42); Pharmacy 14.7% (n=44); Nursing 16% (n=48) and Physical Education 25% (n=75). Of these, 15% (n=45) volunteers used anorexigenic substances at least once in their lives. The most commonly used appetite-suppressing substances were sympathomimetic stimulant drugs (5%), including amfepramone (3.3%) and fenproporex (1.7%). Serotonin reuptake inhibiting substances accounted for 3%, whereas plant extracts were involved in 1.7% of the cases. A miscellanea of other substances accounted for 4.6% of cases. The lifetime use of appetite suppressants was distributed among different undergraduate courses as follows: Nursing 26.7, Nutrition 26.2%, Physical Education and Pharmacy 17.8%, Biology and Physiotherapy 6.7% and Medicine 0%. A two-way contingency table analysis demonstrated a significant correlation between enrollment in specific undergraduate courses and use of appetite suppressants, Pearson  $\chi^2$  (6, N=300)=15.91, p= 0.014, Cramér's V= 0.23.

**Conclusions:** Within this sample, lifetime use of appetite suppressants was significant, being sympathomimetic stimulant drugs the most commonly used agents. Undergraduate Students enrolled in Nursing and Nutrition courses presented significantly higher prevalence of lifetime use of appetite suppressants.

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