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ALPHA-PYRROLIDINOVALEROPHENONE (ALPHA-PVP): SELF-ADMINISTRATION AND ACUTE DRUG CHALLENGES IN RATS.

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Aims: Assess the abuse liability of alpha-PVP (a drug often found in "bath salts") in preclinical animal models of reward/reinforcement and physiology.
Methods: The behavioral and physiological effects of alpha-PVP were assayed in male Wistar rats using both intravenous self-administration (IVSA) and acute drug challenge experiments.
Results: IVSA of alpha-PVP was readily established on a fixed-ratio schedule of reinforcement to stable intake patterns and high lever discrimination. Dose-dependent rates of responding were observed under both fixed-ratio and progressive-ratio schedules that were consistent with alpha-PVP acting as an effective reinforcer/reward. In acute challenge studies, bolus injections of alpha-PVP caused biphasic changes in activity consistent with those of psychomotor stimulants (i.e., increased activity at low doses; suppressed activity with associated stereotypy at high doses).
Conclusions: These data indicate that alpha-PVP has an abuse liability that is similar to that of other stimulant drugs of abuse.
Financial Support: Grants DA024105 and DA024705

2

ADDICTION SERVICES FOR WOMEN IN EASTERN EUROPE: WHAT IS AVAILABLE AND WHERE?

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Aims: This study examined addiction services for women (including pregnant women) in 8 Eastern European countries.
Methods: For 5 countries (Slovenia, Croatia, Czech Republic, Poland and Romania), data from the INSIGHT project were used. INSIGHT collaboratively evaluated addiction treatment facilities, their knowledge and quality of care in these countries (among others). For the remaining 3 countries (Bulgaria, Hungary, Slovakia), questionnaire were obtained about treatment services, with follow-up questions germane to women in general, and pregnant women specifically.
Results: The combined dataset included nearly 100 million people, which represents nearly 70% of the Eastern European population (excluding Russia and Croatia). As expected, drug abuse was more common in males than females. Stimulant use had increased overall, with homemade methamphetamine (pervitine) more prevalent in northern and cathinones (legal highs) more prevalent in southern countries. When IV use was examined, more stimulant use (homemade meth) was seen in Slovakia and Czech Republic (>50%) as compared to Hungary, Romania and Bulgaria (33% cathinones) and finally Slovenia and Croatia (predominantly opioids; some cocaine). Only Slovenia reported addiction programs for women, but described a need for more structured, long-term psychotherapy. No pregnancy-specific addiction programs were found. However, all 8 countries offered opioid substitution services (buprenorphine or methadone) to pregnant women, at no charge. Also, treatment was provided for neonatal abstinence syndrome.
Conclusions: Only in Slovenia were gender-specific services offered to women. For the other 7 countries, improvement is needed as such programs tend to produce better outcomes. In particular, priority should be given to specialized care for pregnant women.
Financial Support: No support

3

GENDER DIFFERENCES IN POLYSUBSTANCE USE AMONG THOSE WHO MISUSE PRESCRIPTION OPIOIDS.

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Aims: This analysis explores gender differences in polysubstance use amongst those who misuse opioids prescribed to them and those who use prescription opioids without a prescription.
Methods: Analyses were conducted on data from 632 community members recruited from college campuses, medical centers, and community centers around the St Louis Metropolitan Statistical area. Participants must have indicated either using prescription opioids in a way other than prescribed, or using prescription opioids that were not prescribed to them in the past 12 months. Multivariate logistic regression was used to determine the association between demographic factors and use patterns of opioids.
Results: Males who reported using prescription opioids without a prescription had higher odds of marijuana and other illicit drug use such as cocaine/crack and ecstasy (AOR 8.0, CI 3.1- 20.0) than males who misused their own prescription opioids. Additionally, males who used opioids without a prescription had higher odds of being arrested more than 5 times (AOR 4.1, 95% CI 1.6- 10.3), being younger (AOR 4.0, 95% CI 1.4-11.3), and reporting less income (AOR 5.2, CI 1.5- 18.3) than males who misused their own prescription opioids. Similarly, females who used opioids without a prescription had higher odds of using marijuana and other illicit drugs (AOR 2.2, 95% CI 1.0- 4.7), as well as having more than 5 arrests (AOR 3.9, CI 1.3- 11.5) when compared to females who misused their own prescription opioids.
Conclusions: Amongst those who misuse prescription opioids, male illicit opioid users had the highest risk for polysubstance use. Overall, the results illustrated key delineations amongst those who illicitly use prescription opioids and those who misuse their own prescription, particularly in males. Future research on the non-medical use of prescription opioids should consider assessing different types of non-medical use, especially in male populations.
Financial Support: R01DA20791, McKnight Doctoral Fellowship

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PRIMARY DRUG USE TYPES AND INTERVENTION-RELATED SELF-MONITORING IN HIV PATIENTS.

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Aims: In HIV primary care patients, drug abuse is a common problem; brief, effective interventions are needed. Self-monitoring is an evidence-based element of brief intervention. In a randomized trial of "HealthCall," a technology-assisted self-monitoring intervention to reduce non-injection drug use (NIDU), patients' primary drug varied, as did their engagement in self-monitoring. A better understanding of patient characteristics associated with primary drug type can help tailor interventions for this population; understanding correlates of patient engagement in HealthCall-assisted self-monitoring can assist counselors in improving personalized feedback, engagement and treatment outcomes.
Methods: In an on-going randomized trial, 200 patients in urban HIV primary care clinics abusing non-injection drugs (stimulants, opioids) have been randomized to control, Motivational Interview (MI)-only, or MI+HealthCall. We examined baseline correlates of primary drug type in the full sample, and predictors of patient engagement (daily call rates) in HealthCall.
Results: Cocaine as the primary drug was associated with greater likelihood of binge drinking ($p=.01$) and Hispanic ethnicity ($p<.04$). Heroin as primary drug was associated with greater age ($p<.0001$) and more years since HIV diagnosis ($p<.0001$). Methamphetamine was associated with greater education ($p<0.001$). The median rate of HealthCall self-monitoring was 67% of 60 possible days. A high HealthCall self-monitoring rate was associated with Hispanic ethnicity ($p<0.03$), greater age ($p=0.006$) and more years since HIV diagnosis ($p=0.04$).
Conclusions: Results indicate differential characteristics associated with primary drug type in HIV primary care, suggesting the importance of tailored interventions. Findings also suggest that Hispanic patients and those with HIV for many years respond especially well to HealthCall technology, which offers promise as a scalable enhancement of brief interventions for non-injection drug use in busy HIV primary care clinics.
Financial Support: R01DA024606, R01AA014323, K05AA014223, and NYSPI

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SEXUAL RELATIONSHIP POWER, VICTIMIZATION, AND HIV RISKY SEXUAL BEHAVIOR IN SUBSTANCE-ABUSING AFRICAN-AMERICAN WOMEN.

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Aims: The goal of the current study was to assess the associations between victimization (physical, adult sexual, and child sexual abuse), sexual relationship power (SRP), and unprotected sex occasions (USO) in substance abusing African American (AA) women. It is hypothesized that SRP moderates the relationship between victimization and USO. Specifically, as SRP increases, the relationship between reported victimization and HIV risk behaviors will decrease.
Methods: The current study was a secondary analysis of baseline data collected from the National Institute on Drug Abuse Clinical Trials Network 0019 (CTN 0019) (Tross, Campbell, Cohen, Calsyn, Pavlicova, Miele, et al., 2008). The CTN 0019 protocol was a multi-site randomized clinical trial that assessed the intervention of Safer Sex Skills Building (SSSB) in women substance abusers on reducing HIV sexual risk. The current study consists of 124 AA women from the CTN 0019 dataset. Participation eligibility required women to be at least 18 years of age, proficient in English, enrolled in substance abuse treatment, and to acknowledge unprotected heterosexual intercourse within the past 6 months.
Results: In the current sample, 70.2% (N=87) endorsed lifetime physical abuse from a male sexual partner. Of the women experiencing physical abuse, 33.3% (N=29) reported physical abuse from their current main partner. Independent sample t-tests showed that women who self-reported physical abuse had lower levels of SRP than those who did not ($t(118)= 3.18$; $p<.01$). The moderation model of SRP decreasing the relationship between victimization and risky sexual behavior approached significance ($p=.064$).
Conclusions: The current study is among the first to examine moderating factors of SRP in substance-abusing African American women. The findings from this study provide evidence that substance abuse interventions may benefit from activities promoting the development of sexual relationship power and self-efficacy in substance-abusing African American women who have experienced victimization.
Financial Support: No financial support was provided for the current study.

6

STRATEGIES TO INFLUENCE ATTITUDES TOWARDS PHARMACOTHERAPIES FOR ALCOHOL AND OPIOID USE DISORDERS.

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Aims: To facilitate the implementation of pharmacotherapies used to treat alcohol and opioid use disorders in specialty treatment.
Methods: Nine treatment centers and a large, commercial health plan created internal change teams to increase patient access to addiction medications. Using bi-annual Learning Sessions, topical webinars, and coaching, sites were trained on medication efficacy and their potential role in increasing patient engagement, retention, and recovery. Sites implemented three 6-month change cycles. Qualitative interviews charted change strategies, change impacts, barriers/facilitators, and patient use of pharmacotherapies.
Results: Incongruity between leadership and staff attitudes inhibited adoption. At one site, staff and physicians were motivated to use medications but faced an abstinence-oriented Board. The staff used education and advocacy, and after a year received Board approval. Another site with progressive leadership faced an abstinence-oriented staff. Data tracking and staff education enhanced staff support for use of medication. When staff and leadership had similar attitudes, the best opportunity existed for the adoption of medications. A progressive staff and research-driven leadership extended their goals and made data tracking part of the agency culture.
Conclusions: Changes in attitude among staff and leadership towards addiction medications occur slowly. The use of strategies that challenge existing attitudes and knowledge encourages change and promotes the organization's adoption of addiction medications. Sites with attitudinal consensus are able to focus on higher-order medication implementation goals while sites with attitude incongruences must first work to achieve attitude alignment.
Financial Support: NIDA Grant R01 DA029716

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ASSESSING STIGMA TOWARDS DRUG USERS AMONG HEALTH CARE PROVIDERS.

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Aims: Stigma involves disapproval and discrimination of individuals with a discrediting mark. Negative beliefs about patients may influence decisions made by treatment providers resulting in suboptimal care.Assessing the impact of stigma and contribution to health disparities requires valid measures of drug abuse stigma in health professionals. We report the need for stigma research in treatment, the adaptation and validation of a stigma measure for providers translated from English to Spanish, and correlates of stigma, in a sample of Puerto Rican health profession students and practicing professionals.
Methods: Anonymous questionnaire was administered to 474 grad students and 186 practicing professionals in Medicine, Nursing, Psychology, and Social Work in Puerto Rico. Data was collected for socio-demographic variables and experiences with individuals with substance use disorder. A translation and adaptation of the Community Attitudes towards Substance Abuse (CASA) scale developed by researchers at U of Nevada Reno was included. Rasch analysis was conducted with each dimension of the CASA scale as sub-tests and bivariate analysis to explore the correlates of stigma.
Results: The data fit the Rasch model. Stigma varied significantly by discipline. All scores fluctuated slightly under the midpoint of the scale. Higher scores were obtained for nurses, followed by physicians, psychologists, and social workers ($P<.01$). Stigma levels remained stable between students and professionals within disciplines. Stigma was signifcantly associated to drug use problem among patients in professional's practice ($p<.03$) and among relatives ($p<.02$).
Conclusions: CASA is a valid instrument that can be used for Latino and English speaking providers to further research on stigma. Stigma in this sample does not change with academic progress or experience in the workforce suggesting that academic and professional training on countering stigma is either absent or ineffective. Implications for professional training, for theory building and for the research on the impact of stigma in clinical care will be discussed.
Financial Support: NIDA Grant #1R24DA024868-01A2

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OXYTOCIN EFFECTS ON HUMAN AGGRESSIVE RESPONDING.

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Aims: In the search for interventions aimed at improving the social functioning of individuals with substance use disorders (SUD), the neuropeptide oxytocin (OT) and the oxytonergic system may hold promise as an intervention strategy for promoting prosocial behaviors. Acute administration of OT has been shown to increase cooperation, trust, and generosity adult humans. These behaviors are labeled prosocial and stand in contrast to aggression, which may be considered antisocial. In addition to prosocial effects of OT administration, OT dose has been shown to facilitate social cognition in individuals with disorders characterized by deficits in social behavior and cognition. Individuals with a history of SUD have higher rates of aggressive behavior and a direct effect of OT dosing on human aggressive behavior has yet to be clearly experimentally demonstrated, this study seeks to examine the potential impact of OT on aggressive behavior in humans. The primary hypothesis is that acute administration of OT dose will decrease human aggressive behavior.
Methods: In this ongoing study, subjects participate in a within-subjects repeated measures design. All subjects receive placebo and 24 international units of OT. Human aggression is measured using the Point Subtraction Aggression Paradigm (PSAP), a laboratory method with demonstrated sensitivity to acute drug effects. Dependent measures include the rate of aggressive responding on the PSAP and clinically relevant personality traits to examine possible associations with OT response.
Results: Currently, we have completed eight subjects. Preliminary analyses indicate a positive association between OT-mediated changes in aggressive response rate and pathological personality traits.
Conclusions: Individual differences in response to acute OT administration appear to be related to level of trait aggression and/or pathology, providing clinical implications for use of OT in individuals with SUD.
Financial Support: National Institute of Drug Abuse
National Institute of Health

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EVALUATION OF THE EFFECTIVENESS OF DRUG PREVENTION PROGRAMS: ANALYSIS OF THE INTERNATIONAL SCIENTIFIC PRODUCTION (2002-2011).

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Aims: The objective was to analyze the international scientific production in the period 2002-2011 of articles that assess the effectiveness of drug use prevention programs by means of bibliometric methods through the Web of Knowledge and Scopus databases.
Methods: We perform bibliographic searches in the Web of Knowledge and Scopus databases. We use bibliometric methods to identify the scientific production and collaboration.
Results: The number of selected articles was 253, with a progressive evolution of the number of published articles during those 10 years, from 21 in 2002 to 38 in 2011. The articles have 942 different authors, where 819 (86.94%) published a single paper. The average number of authoring was 4.55, which indicates the degree of collaboration. The top four productive institutions are American, with more than 10 published articles about this topic, and some European institutions. The Latin America production was lower. Most of the production (237, 94%) was published in English and only 14 in other languages (9 in Spanish, 4 in German, 2 in Slovakian and 1 in Portuguese).
Conclusions: The results show that collaborations are like a threesome shape, with one country from North America, an European country and a third country from another continent), demonstrating that international scientific collaboration in the area have multiple networks and profiles. This is the case of the United States, representing the core of most of the networks.
Financial Support: Plan Municipal de Drogodependencias. Concejalía de Sanidad y Consumo. Ayuntamiento de Valencia. Spain.

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GAMBLING BEHAVIOR AMONG GAMBLERS WITH AND WITHOUT ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

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Aims: Previous studies showed that Substance Use Disorder (SUD) and Attention Deficit/Hyperactivity Disorder (ADHD) often co-occur. However, few studies have investigated relationships between ADHD and gambling disorder. The aim of this study was to assess the characteristics of gambling among gamblers with and without ADHD.
Methods: 599 gamblers (66% males, 43 y.o.) were recruited in addiction clinics and gambling places in France. Subjects were interviewed with standardized questionnaires to assess ADHD symptoms in childhood and adulthood, gambling characteristics (gambling habits, DSM-IV criteria for pathological gambling, gambling severity, and related cognitive distortions) and psychopathology.
Results: 20.7% (n=124) of gamblers presented a lifetime or current ADHD. Exhibiting ADHD was associated with a greater risk to exhibit problem gambling, with a higher severity of gambling-related problems, to exhibit cognitive distortions related to gambling, and psychiatric comorbidities (p<.0001).
Conclusions: ADHD was highly prevalent among gamblers, and it was associated with more severe gambling disorder. Improving ADHD screening among gamblers would improve the treatment of gambling disorder.
Financial Support: : MILDT-INSERM 2007

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CANNABIS USE AMONG WOMEN AND DURING PREGNANCY.

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Aims: Exploring the potential management of cannabis among women and during pregnancy, an expanding public health issue.
Methods: A Medline search from 1980 – 2013 for articles highlighting drug abuse among women and during pregnancy, with particular emphasis on cannabis/ marijuana use during pregnancy, delivery and its management as well as the drug impact on the fetus.
Results: Cannabis is the most commonly used illicit drug among youth and pregnant women in western societies. Historically, cannabis has been used to alleviate nausea during pregnancy. In reviewing the literature on the use of medication as well as psychosocial approaches in women and pregnancy, clinical guidelines emerge as well as a research agenda including prevalence estimates through urine screening. The implication of a positive test should not be punitive. clinical trials on pregnant samples should also be conducted. The impact of THC and other cannabinoids should be further investigated as well as support of the newborn and developing child.
Conclusions: Compared to the preventive efforts targeting alcohol and tobacco use during pregnancy, the increasingly common use of cannabis is relatively neglected and in need of further specific investigations.
Financial Support: No financial support was received.

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DISTRESS TOLERANCE MODERATES THE RELATIONSHIP BETWEEN SOCIAL REJECTION AND MAJOR DEPRESSIVE DISORDER IN INNER-CITY SUBSTANCE USERS.

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Aims: Social rejection contributes to depression. Given the high rates of comorbidity between substance use and depression, it is imperative to understand factors influencing the relationship between social rejection and depression in substance users. Distress tolerance, defined as the ability to withstand negative emotional states, may underlie this relationship. The current study explored whether distress tolerance moderates the association between social rejection and depression in substance users. We hypothesized that the positive relationship between social rejection and depression would be evident only among those with low distress tolerance.
Methods: The present study included 72 substance users (84.72% male) receiving inpatient substance abuse treatment. The dependent variable, major depressive disorder, was diagnosed using the Substance Dependence Module of the Structured Clinical Interview for DSM–IV. The main independent variable, social rejection, was elicited and assessed through a virtual ball-toss game, Cyberball. The moderator, distress tolerance, was self-reported using the Distress Tolerance Scale.
Results: Logistic regressions indicated a significant interaction between social rejection and distress tolerance in predicting depression in substance users (Wald = 4.63, $p < 0.05$). Probing of this interaction indicated that social rejection was significantly associated with depression among substance users with low distress tolerance (Wald = 4.58, $p < 0.05$), but no relationship was evidenced among those with high distress tolerance (Wald = 0.95, $p > 0.05$).
Conclusions: Findings of the study indicate that low distress tolerance is associated with a risk for depression in the context of social rejection in substance users. Depression treatments and interventions may benefit by incorporating distress tolerance skills to reduce depression among substance users who experience social rejection.
Financial Support: Research supported by grant from the National Institute of Health (RO1DA026424).

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GENDER DIFFERENCES IN USE OF ALTERNATIVE TOBACCO PRODUCTS AMONG DAILY AND NONDAILY SMOKERS.

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Aims: We explored gender differences in alternative tobacco products (ATP) use among daily (DS) and nondaily (NDS) smokers. We hypothesized that within each group, men would have higher odds of ATP use compared to women.
Methods: This project is a secondary data analysis from a cross-sectional online survey of 2376 smokers. Participants were either DS (≥ 1 cigarette/day on ≥ 25 days of last 30 days) or NDS (≥ 1 cigarette/day on ≥ 4-24 days of last 30 days). Survey questions included demographics and use of ATP in past 30 days (yes/no), including cigars, cigarillos, little cigars, pipes, smokeless tobacco, hand-rolled cigarettes, hookah, and electronic cigarettes. Statistical analyses included logistic regression models, adjusting for education and employment when necessary.
Results: The DS group contained 1175 participants (60% women) and the NDS group contained 1201 participants (56% women). Men were at higher odds of reporting use of most forms of ATP; ORs ranged from 1.38 (95% CI: 1.04-1.83) for hand-rolled cigarettes among the DS group to 4.10 (95% CI: 2.47-6.82) for smokeless tobacco among the NDS group. Two exceptions were noted. First, in terms of electronic cigarettes, a significant interaction was identified such that within the DS group the prevalence of use was higher in the women (10% vs. 6%) whereas in the NDS group the prevalence was higher in men (12% vs. 7%; p=0.0004). Second, there were no gender differences in use of hookah.
Conclusions: Men were at higher odds of reporting use of most forms of ATP than women in both the NDS and DS groups. Data also suggest that women who smoke daily and men who do not smoke daily may be more likely to use electronic cigarette. Additional research is needed to explore the effect of ATP use on smoking cessation.
Financial Support: Pfizer's Global Research Awards for Nicotine Dependence, NCMHD/NIH 1P60MD003422 and Masonic Cancer Center

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CHANGES IN CIGARETTE AND ALCOHOL USE DURING CANNABIS ABSTINENCE.

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Aims: This study tests if cannabis is substituted with alcohol and/or tobacco during cannabis abstinence, and factors predicting such substitution.
Methods: A prospective community based study quantified cannabis, alcohol and tobacco use with Timeline Follow-back during a two-week voluntary cannabis abstinence and at one-month follow-up in non-treatment seeking cannabis users (n=45). Cannabis use was verified by urine THC-COOH levels.
Results: Overall alcohol use increased by 8 standard units (SU; d=0.48) per week and cigarette use by 14 cigarettes per week (d=0.29) during the two-week cannabis abstinence, with greater increases for those using less of each substance at baseline (alcohol P<0.0001, tobacco P=0.01). There was an overall decrease in alcohol (-4.8 SU, d=-0.29) and tobacco (-13 cigarettes/week, d=-0.26) at follow-up. Increased cigarette use was also predicted by the more severe withdrawal symptoms of insomnia (P=0.05), restlessness (P=0.03) and physical symptoms (P=0.02). Importantly, neither alcohol nor cigarette use increased significantly in those who remained abstinent from cannabis through to follow-up.
Conclusions: Despite concerns that abstinence from cannabis use might drive increased alcohol and cigarettes use this was not supported among those individuals who remained abstinent beyond the acute period of cannabis withdrawal, nor did tobacco use increase in those experiencing milder cannabis withdrawal symptoms. Future research on substitution in treatment seekers during outpatient cannabis abstinence is needed.
Financial Support: Funding was provided by the Australian Government Department of Health

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DIABETES MELLITUS OUTCOMES: IS CANNABIS SMOKING PROTECTIVE?

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Aims: Several diabetes mellitus (DM) research teams have investigated whether cannabis smoking might influence DM outcomes. Inverse associations have been found, more consistent with the idea that cannabis smoking might confer protection, perhaps via immunomodulatory effects on oxidative stress and inflammation pathways leading toward these outcomes. Our main aim is to add new epidemiological estimates to this body of research, with an advance expectation of the inverse association reported by others.
Methods: Self-report data on cannabis and DM are from IRB-approved self-interviews of adult participants for the 2005-2012 US National Surveys on Drug Use and Health (NSDUH; n=243,012), as well as the 2005-2012 National Health and Nutrition Examination Survey (NHANES; n= 12,677). NHANES also considered glycosylated hemoglobin level (HbA1c) ≥ 6.5%, and oral hypoglycemic medication or insulin. Odds ratio (OR) estimates of the associations are from multiple logistic regression, with due attention to complex survey design and weights.
Results: Compared to never users, the OR for an cannabis-DM association among recently active users is 0.6 (95% CI = 0.5, 0.7) in NSDUH and 0.6 (95% CI = 0.4, 0.8) in NHANES. Estimates changed little with covariate adjustment or with inclusion of serum and/or medication indicators; no strong OR subgroup variation was found.
Conclusions: Cannabis smoking is inversely associated with DM outcomes, independent of potential confounders studied here. Cannabinoid protection may be involved, but new prospective and experimental studies are needed. Pre-clinical research (e.g., in a CBD knockout mouse model) may help clarify potential anti-inflammatory and endocrine-disrupting pathways.
Financial Support: Supported by NIDA T32DA021129 (OA); K05DA015799 (JCA).

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FAMILY HISTORY OF DRUG PROBLEMS AS A MARKER FOR OTHER HEALTH RISKS IN PRIMARY CARE PATIENTS.

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Aims: The study aim is to determine whether risk behaviors and mental health history differ by family history of drug problems.
Methods: N = 3,253 participants were recruited from the waiting room of a hospital-based primary care clinic as part of a larger drug and alcohol Screening Brief Intervention and Referral to Treatment (SBIRT) study. Using a small tablet computer in the clinic waiting room participants completed an interactive, computer-delivered screening and assessment, including questions about demographics, mental health history, partner violence exposure, substance use behaviors and family history of substance use. Participants were classified into 4 groups based on their report of family members' history of problems with drugs: 1) no family history; 2) second degree only (grandparents); 3) first degree only (parents and siblings); and 4) first and second degree. Logistic regression analyses were used to compare the four groups on multiple risk factors, with no family history as the reference group. Age, gender, and race were added as covariates in adjusted models.
Results: Participants were predominantly mid 40's (mean 46.6, SD 12.25), women (73%), and Black (72%). Family history of drug problems was associated with current smoking [1° AOR 1.8 (1.54, 2.11)], positive alcohol CAGE [1° AOR 2.6 (2.02, 3.36); 1° & 2° AOR 7.5 (3.72, 15.21)], positive drug CAGE [1° AOR 4.2 (3.06, 5.76); 1° & 2° AOR 7.0 (3.04, 15.99)], past year violence victimization [1° AOR 1.8 (1.37, 2,28); 1° & 2° AOR 5.5 (2.99, 10.08)], and previous diagnoses of anxiety [1° AOR 1.8 (1.37, 2,28); 1° & 2° AOR 5.5 (2.99, 10.08)] and depression [1° AOR 1.8 (1.37, 2,28); 1° & 2° AOR 5.5 (2.99, 10.08)].
Conclusions: Family history of drug problems is associated with increased odds for substance use, violence exposure, and mental health diagnoses in primary care patients. This risk appears additive as high density family history of drug problems (first and second degree relatives) was associated with the highest risk.
Financial Support: RO1 DA026091, 5K23AA020316-02

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A COMPARISON OF OUTCOMES BY SEXUAL ORIENTATION AMONG WOMEN IN INTEGRATED SUBSTANCE USE AND MENTAL HEALTH DISORDER TREATMENT.

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Aims: There is limited research on the treatment of addiction and mental health disorders among sexual minority women. We compared outcomes of heterosexual, lesbian, and bisexual participants in the Women, Co-Occurring Disorders and Violence Study, a nine-site quasi-experimental longitudinal study that compared integrated treatment for substance use, mental health, and trauma with services-as-usual (N = 2,729).
Methods: Mixed-effect models were fitted for each outcome (alcohol and drug severity, alcohol and drug abstinence, mental health symptomatology, trauma symptomology, and interpersonal traumatic events exposure during the previous 6 months). Three-way interactions tested whether the integrated treatment was equally efficacious across sexual orientation groups. Pairwise comparisons were performed to assess differences among sexual orientation groups.
Results: Significant three-way interactions for alcohol and drug severity and mental health symptomatology ($p < .05$) indicated that differences by condition over time varied by sexual orientation. Among participants in the intervention condition, lesbians had smaller reductions in alcohol severity scores, bisexual women had greater reductions in drug severity scores, and heterosexual women had greater reductions in mental health symptoms compared to individuals receiving usual care. No differences between conditions were found across sexual orientation groups for other outcomes.
Conclusions: Alcohol and drug severity and mental health symptomatology outcomes varied across sexual orientation groups. Implications for future research are discussed.
Financial Support: Supported by the Substance Abuse and Mental Health Services Administration, Department of Health and Human Services (grant no. 1 UD1 TI-11397).

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EPIGENETIC REGULATION OF CORTICAL SEROTONIN (5-HT) 5-HT_{2A}:5-HT_{2C} RECEPTOR BALANCE IN MALADAPTIVE IMPULSIVITY.

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Aims: Impulsivity factors into the multifaceted determinants that underlie the etiology of substance use and obesity/eating disorders. Prevention and treatment of these chronic pathological maladies could be greatly advanced by a more comprehensive understanding of the biology of impulsivity. Neural function is regulated by a myriad of regulatory epigenetic, transcriptional, translational and topological processes. Considerable evidence indicates 5-HT systems play a role in impulsivity through the 5-HT_{2A} receptor (5-HT_{2A}R) and 5-HT_{2C}R within the medial prefrontal cortex (mPFC). We tested the hypothesis that impulsivity is dynamically controlled by a cortical 5-HT_{2A}R:5-HT_{2C}R homeostasis and that epigenetic factors may contribute to individual differences.
Methods: Impulsivity was evaluated in rats using the 1-choice serial reaction time task; mPFC was extracted from rats characterized as high or low impulsive and processed for DNA, RNA or protein analyses. DNA was subjected to epigenetic PyroMark sequencing to assess methylation patterns of the 5-HT_{2A}R and 5-HT_{2C}R genes. We employed immunoblots to detect mPFC synaptosomal protein expression of the 5-HT_{2A}R and 5-HT_{2C}R.
Results: Levels of impulsivity positively correlated with 5-HT_{2A}R protein levels (R^2=0.21;$p<0.01$), inversely correlated with 5-HT_{2C}R protein levels (R^2=0.22;$p<0.01$) and positively correlated with 5-HT_{2A}R:5-HT_{2C}R ratio (R^2=0.31;$p<0.01$). Methylation of 5-HT_{2A}R did not associate with impulsivity; 5-HT_{2C}R was methylated to a greater degree in high vs. low impulsive rats ($p<0.05$).
Conclusions: These data indicate that there is an interactive relationship between mPFC 5-HT_{2A}R and 5-HT_{2C}R that may drive impulsive phenotypes. Methylation patterns of these genes may mediate a gene x environment interaction to control inherent impulsivity, such that high impulsivity associates with higher 5-HT_{2C}R methylation in a critical brain region linked to impulsivity. Thus, we have uncovered potential neurobiological mechanisms of importance in driving inherent impulsivity.
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WORKFORCE ATTITUDES REGARDING THE IMPLEMENTATION OF EXTENDED RELEASE NALTREXONE TO TREAT OPIOID DEPENDENCE.

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Aims: Prior research indicates that organizational and workforce characteristics influence the implementation of evidence-based treatments. This study examined the workforce's response to the utilization of extended release naltrexone to treat opioid addiction at time one (n=36) and time two (n=30). It explores staff opinions toward the implementation of a new medicated assisted treatment (MAT) for opioid addiction and documents the integration of an FDA approved treatment in an in-patient addictions facility.
Methods: A mixed-methods approach was employed using semi-structured interviews and a quantitative survey with the staff at the addictions facility. Participants were support staff who interacted with patients. The quantitative survey was administered early in the new MAT program implementation (n=36) and again six months later (n=30). Data was analyzed using STATA and included descriptive statistics, correlations t-tests, and analyses of variance. Atlas-ti software was used to analyze codes in the qualitative data regarding attitudes and opinions about MAT.
Results: Data from the survey suggest that over time, workforce knowledge about the new MAT increased (33.33% to 77.78%). There was also a slight increase in workforce opinion that their coworkers supported the use of the new MAT (11.11% to 51.85%) as well as opinion that their supervisors supported the new MAT (48.57% to 70.37%), indicating an increase in perceived social support. The qualitative data indicate the importance of housing and peer support to successful recovery.
Conclusions: Our findings indicate that counselors and support staff play a critical role in the adoption of efficacious MATs, with perceived social support at time two ranging from 51.85% for supervisors and 77.78% for coworkers. Greater attention to staff attitudes and perspectives when working to accelerate utilization of medications are recommended for improved patient outcomes.
Financial Support: This work was supported by the Hooper Detoxification Stabilization Center Vivitrol® Pilot Program State Funded Evaluation Project.

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A REMOTE WIRELESS SENSOR NETWORK/ ELECTROCARDIOGRAPHIC APPROACH TO DISCRIMINATING COCAINE USE.

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Aims: To establish the sensitivity/specificity of a RWSN/ECG approach for discriminating cocaine use from other cardiovascular stimulants. Hypothesis: Wearable "on body" sensors will reliably distinguish cocaine-induced ECG changes from those induced by methylphenidate (MPH) and exercise.
Methods: Subjects: Five experienced cocaine users (4 male / 1 female; 41 ± 8 yrs; lifetime cocaine use = 17 ± 9 yrs).
Procedures: Subjects wore the Zephyr BioHarness 3 chest band (left mid-axillary line) during 180 min of self-regulated IV cocaine administration (8, 16, and 32 mg/70kg), for 90 min after a single 45 mg dose of oral MPH, and during 15-30 minutes of aerobic exercise (ping pong or stationary bike) on an inpatient research unit.
Statistical Analyses: 1. A computational pipeline was used to preprocess ECG data and identify ECG (P, Q, R, S and T) peaks. We extracted two types of features: one, PQRST waves (waveform features); two, all morphological (AM) features (PR, QRS, QT and QTc intervals), following which a binary classification model (logistic regression) was assessed for its ability to distinguish between conditions (cocaine vs. MPH; cocaine vs. exercise). Classifier performance was expressed as Area Under Receiver Operating Characteristics curve (AUROC).
Results: Classifiers consistently distinguished cocaine use from exercise (N = 5) and MPH (N = 4) with mean AUROC of > 0.9 and > 0.95 for AM and waveforms, respectively.
Conclusions: If sensitivity/specificity of RWSN/ECG approach (>90 %) is confirmed in larger outpatient cohorts, such methods may be of value in medication development efforts (i.e., clinical trials) for cocaine.
Financial Support: Supported by:
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WITHDRAWN

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COMPARISON OF SYNTHETIC SUBSTANCES: DIFFUSION OF INNOVATION FRAMEWORK.

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Aims: Synthetic cannabinoids (SCann) and synthetic cathinones (SCath) represent new challenges for law enforcement and regulators. We investigated the use of SCann and SCath in one U.S. geographic region (1.5 million people) using Roger's Diffusion of Innovation framework.
Methods: Mixed methods including analysis of 24 month treatment admissions, surveys of substance abuse treatment providers (n=16), and qualitative interviews conducted with a purposive sample of out-of-treatment (n=10) and in-treatment participants (n=14).
Results: The user system norm supported trying new drugs, and both drugs were confirmed to be available in the environment. For the innovation-decision process, knowledge was greater for SCann than SCath as SCath was viewed as causing harm and users were unsure how to ingest it. In contrast SCann was compatible with known drug (i.e., marijuana) and used similarly. Both SCann and SCath were viewed as accessible and inexpensive (i.e., high trialability). The persuasion stage also favored SCann as almost all the users knew someone who had used SCann but few knew anyone who had used SCath. These differences lead to greater implementation of SCann than SCath as evidenced by total admissions, substance abuse treatment providers' survey, and users' experiences. However, after SCann and SCath were removed from shelves due to community mobilization, health alert, and Scheduling, there was disenchantment discontinuity in the confirmation stage. Few users expressed ongoing demand for synthetic compounds (either SCann or SCath) if they were not easily available and legal. All users expressed preference for what they called "real" drugs, indicating SCann and SCath had no relative advantage over other drugs of abuse.
Conclusions: This qualitative study showed SCann and SCath experienced different and declining demand in this region. Diffusion of Innovation provides a framework for understanding the differential use of substances and subsequent decline.
Financial Support: Funding was provided by grants from Southeast Michigan Community Alliance and the state of Michigan (Lycaki-Young funds).

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USING DATA MINING OF SPONTANEOUS ADVERSE EVENT REPORTS AND MULTIVARIATE STATISTICAL METHODS FOR ASSESSING ABUSE POTENTIAL.

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Aims: To further evaluate the usefulness of data mining methods and other multivariate analyses as tools for characterizing abuse potential and monitoring for signals of abuse in spontaneous adverse event reports.
Methods: A data mining/disproportionality analysis (DA) of CNS-acting drugs in the FDA AERS database based on 2x2 contingency tables was performed. The analysis used a prespecified list of adverse event (AE) terms associated with drug abuse and drugs were grouped based on DEA scheduling level (including selected nonscheduled products). In addition, the results of the individual AE terms were supplemented with pooled case definitions based on groupings of AEs with similarconstructs and groupings of drugs by pharmacological class. Comparisons of the patterns of statistic of disproportionate reporting (SDRs) for these AEs were made among nonscheduled drugs and drugs of Schedules II-V. Subgroup analyses based on age and gender were also performed. EB05>2 was used as the threshold for SDRs. Additional analysis of the relationship between drugs and events in multi-dimensional space was performed using multivariate methods such as cluster and correspondence analyses.
Results: Overall, DA analysis showed that the number and type of AEs (overt abuse/misuse (OAM) vs mood/mental state AEs (MMS))and strength of SDRs varied between drug groupings, with higher level schedules showing stronger SDRs for OAMs and lower level schedules showing stronger SDRs for MMS. The analysis by gender in general showed overlapping or similar SDRs by schedule level, though there was differentiation for some AEs in some drug groups. Similar results were seen with the age-based subgroups.
Conclusions: Data mining spontaneous AEs may be useful as a tool for prospectively monitoring abuse of marketed drugs, though the methods are as yet unvalidated. Used retrospectively, data mining and multivariate statistical methodologies maybe of value in identifying patterns of drug-event combinations not otherwise apparent, which can serve to better characterize abuse potential.
Financial Support: This research was funded by Pfizer Inc

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COMPARATIVE EFFICACY OF A COMPUTER-BASED HIV TESTING VIDEO INTERVENTION IN SITES OF VARYING HIV PREVALENCE.

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Aims: To examine the comparative efficacy of a computer based video intervention intended to increase HIV test rates among emergency department (ED) patients at two sites.
Methods: 160 patients who initially declined HIV testing at two high volume Manhattan EDs used inexpensive handheld computers to view a brief (<16 minute) intervention that included an automated substance use screening and the offer of an HIV test. One ED serves an exceptionally high HIV prevalence area (>4%) the other ED serves a lower prevalence area. Chi-square analyses examined test rates, reported substance use (both current and/or problematic), and participant race by ED testing site.
Results: Patients at the ED serving higher HIV prevalence areas were significantly more likely to test following the intervention than participants in the ED serving lower HIV prevalence areas (43.8% versus 25.6%, $\chi 2 = 5.70$, $p = .017$). No significant differences were found between sites in the race of participants, or in reported substance use among the study sample.
Conclusions: The computer based HIV testing video intervention was more efficacious in areas of higher HIV prevalence. It remains unknown whether testing rates were higher because participants felt they were at greater risk, or for other reasons. Additional research is warranted to further optimize interventions for people in high-risk neighborhoods as well as those in lower risk areas.
Financial Support: NIDA R03 DA031603
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PRECLINICAL EFFICACY OF AN ANTI-METHAMPHETAMINE VACCINE WITH AN E6020 ADJUVANT.

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Aims: Prior research in our group showed that methamphetamine (MA) vaccines constructed with an Alum adjuvant are capable of producing anti-MA antibodies that increase greatly after 1-2 boosts in mice. This vaccine schedule also led to decreased behavioral effects of MA. Now, we test a vaccine formulated with E6020, a Toll-like receptor-4 agonist, to determine if it produces anti-MA antibodies and alters behavioral effects of MA in mice.
Methods: We determined the optimal dose of E6020 (0-10ug) that generates an efficacious antibody response. This dose (3mg) was then used to construct a vaccine made from a combination of E6020 and Alum (1.5mg) adjuvants with 32mg of tetanus toxoid (TT)-succinyl methamphetamine (SMA). Female BALB/c mice (n=30) were vaccinated with TT-SMA and boosted at weeks 3 and 6 and 30 other mice served as unvaccinated controls. Vaccine groups were divided into 3 groups (n=10 ea) to test behavioral effects of MA (0, 0.5, or 2.0 mg/kg). After the first boost, the locomotor effects of MA were assessed by measures of horizontal and vertical activities in a 60-min session. After the second boost, a conditioned place preference (CPP) study was initiated. Using an unbiased procedure and maintaining MA dose assignments, mice were given 4 conditioning trials (30-min) each of MA and saline on alternating days in which they were confined to one conditioning side. The CPP test (30-min) was conducted drug-free and times spent in the drug- vs. the vehicle-paired side were determined.
Results: Peak antibody levels increased 2-fold with the optimal E6020 dose versus alum alone. Horizontal activity decreased significantly in vaccinated groups, particularly at the high MA dose, $P<0.0001$. No effect was seen with vertical activity. MA supported CPP but no significant effect of vaccine was observed.
Conclusions: Results suggest that anti-MA vaccines made with the novel adjuvant, E6020, greatly enhance the efficacious production of anti-MA antibodies and have functional consequences.
Financial Support: DP1DA033502

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LONGITUDINAL PATTERNS OF ECSTASY AND OTHER DRUG USE AMONG YOUNG ADULTS.

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Aims: Although recent increases in emergency department visits related to ecstasy (MDMA) have been noted, few cohort studies have examined trends in ecstasy use over time. This study measures ecstasy use in a well-characterized longitudinal sample of young adults and analyzes this behavior in the broader context of alcohol and other drug use.
Methods: Participants were 1,253 young adults (608 men) who were originally enrolled in the longitudinal College Life Study as first-year college students attending one large public university. Data were gathered via eight interviews administered annually regardless of continued college attendance. Lifetime and past-year frequency of use were assessed for ecstasy and 11 other illicit and nonmedically used prescription drugs, along with self-reported DSM-IV criteria for alcohol and marijuana use disorder (AUD, SUD). An index was computed for the number of drugs other than ecstasy that were used at least once during the past year.
Results: Lifetime prevalence of ecstasy use quadrupled from 3.2% in the first year to 12.6% seven years later, with annual prevalence estimates between 1.9% and 4.4%. Past-year frequency of use ranged from 1 to 70 days, but was typically <5 days. Mean frequency of use was stable at approximately 3 days through Year 5 and increased thereafter to 8.2 by Year 8. Compared with non-users of ecstasy, ecstasy users consistently used an average of nearly 3 more other drugs—primarily marijuana, cocaine, and hallucinogens. Use of ecstasy in the absence of other drugs was rare (<4% of ecstasy users annually). Both AUD and SUD were highly prevalent among ecstasy users (>70% in some years) and consistently greater than among non-users.
Conclusions: Ecstasy use increased over time among this sample and was a strong indicator of other drug involvement. More research is needed to understand the long-term physiological and behavioral impacts of such use.
Financial Support: National Institutes of Health, National Institute on Drug Abuse: R01-DA014845, Dr. Arria, PI

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EVALUATION OF THE RELATIONSHIP BETWEEN PAIN LEVEL AND CRAVING OF PRESCRIPTION OPIOIDS.

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Aims: Research suggests that craving is a factor that maintains prescription opioid use in opioid-addicted pain patients. The current study was designed to assess the association between pain and craving using a multi-dimensional measure of craving. The study also examined the relationships between craving and various drug use characteristics.
Methods: Patients who preferred prescription opioids as their primary drug of choice were recruited from three different drug treatment centers. Participants completed the Desire for Drugs Questionnaire (DDQ) and the dot probe task to assess craving and attentional bias, respectively. Participants then were administered a battery of questionnaires.
Results: Multiple regression analyses revealed that pain severity was significantly associated with desire-and-intention to use prescription opioids, but not with craving for relief from negative states. Furthermore, preoccupation and intrusive thoughts about prescription opioids, negative meta-cognitions about craving, and outcome expectancies of pain relief from prescription opioids were significantly associated with craving.
Conclusions: These findings are consistent with previous studies reporting a significant positive relationship between pain and craving. Results also provide support for cognitive behavioral models of addiction that hypothesize that craving is associated with negative meta-cognitions about craving and intrusive thoughts about prescription opioids. In addition, this study provides mixed support for negative reinforcement models of addiction which suggest that individuals crave drugs to reduce negative experiences. The DDQ provides a more comprehensive measurement of craving relative to single-item rating scales.
Financial Support: This study was supported by funds from the APF COGDOP Graduate Student Research Scholarship, APA Dissertation Award, and Katzner Graduate Student Research and Professional Development award.

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INITIAL VALIDATION OF A MARIJUANA PURCHASE TASK.

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Aims: A reliable measure of the relative economic value of marijuana is needed to inform and impact the evolving national drug policy on marijuana. Relative value, or demand, for a drug can be measured via a purchase task (PT). Indices of demand from alcohol and cigarette PTs have been significantly associated with craving, dependence, and treatment response (MacKillop & Murphy, 2007; MacKillop et al., 2008; Murphy & MacKillop, 2006). This study examined the demand for marijuana with a marijuana purchase task (MPT).
Methods: The 22-item self-report measure was administered to 104 marijuana users (mean age=21.3, SD=4.3; 36.5% female; 14.4% cannabis dependent; mean possible marijuana use days=71.86%, SD=21.50%).
Results: Pearson correlation analyses indicated a significant negative relationship between Intensity (consumption at zero cost) and age of regular use ($r=-0.32$, $p<0.01$), and significant positive associations with marijuana use days ($r=0.24$, $p<0.05$) and craving ($r=0.43$, $p<0.01$). Omax (maximum expenditure) was positively associated with marijuana use days ($r=0.30$, $p<0.01$) and craving ($r=0.24$, $p<0.05$). Income was not associated with demand indices. An exponential model of demand provided an excellent fit to the data ($R2=0.98$). Users with cannabis dependence symptoms showed significantly more inelastic demand (insensitivity to price increase) than users without current dependence symptoms ($F=181.9$ [df=1, 39], $p<0.001$).
Conclusions: These results provide initial support for construct validity of the MPT, indicating its sensitivity to the relative value of marijuana as a function of increasing cost, and its ability to differentiate between non-dependent users vs. those at greater risk for cannabis dependence. The MPT may help determine price sensitivity and abuse liability across disparate regulatory environments, subjective drug states, and within user subgroups.
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THE MEANING OF WORK: PERCEPTIONS AMONG PERSONS WITH MAINTENANCE TREATMENT FOR OPIOID ADDICTION WHO ARE EMPLOYED.

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Aims: The aim is to explore the experiences of individuals who were employed while undergoing maintenance treatment for opioid addiction with regard to the perceived meaning of work.
Methods: Semi-structured telephone interviews with 32 persons who were employed during maintenance treatment for opiod addiction. Transcripts were analyzed using content analysis.
Results: Apart from the chance to receive maintenance treatment, all informants regarded work as an indispensable tool for staying drug-free and for personal development. Work gave structure to their days, was utilized as a coping strategy and promoted a healthy lifestyle. Social contacts at work were viewed as role models who could support the transition from an identity as a "junkie" into the role of the average "Swede". Work provided an opportunity to develop self-confidence and self-esteem and contributed to an improved social and economic stability. Many obstacles to personal development were reported and described in the interviews as well. Obstacles to personal development were the need to avoid old networks, the continuing stigma of being seen as a "junkie" and the demands of the treatment program itself.
Conclusions: This study provides evidence of the importance people receiving maintenance treatment for opioid addiction place on their employment situation. All of the informants considered work to be an indispensable tool for maintaining their sobriety, as well as a resource for building a new drug-free identity. There is a need for further study of the potential for individual vocational support models to be integrated into maintenance treatment programs.
Financial Support: None

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QUININE: A POTENTIAL TRACER FOR MONITORING MEDICATION ADHERENCE.

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Aims: Clinical trials evaluating pharmacotherapies for substance use disorders can be undermined by medication non-adherence, and sensitive biological adherence markers are lacking. Quinine, marketed as an anti-malarial, was explored here as a potential adherence tracer. The primary aim was to characterize the quinine pharmacokinetic profile in plasma and urine with once daily dosing. A secondary aim was to examine and exclude potential pharmacokinetic interactions with a model hepatically metabolized medication (and common drug of abuse) oxycodone.
Methods: Healthy, non-dependent opioid abusers (n=10) were enrolled in this within-subject, double blind, placebo-controlled, inpatient study. Three 7.5 hr sessions were completed (Days 1, 4 & 5) with dosing as follows: Day 1: 30 mg, p.o. oxycodone, Days 2-4: quinine (80 mg, p.o.), Day 5: quinine and oxycodone 2 hr later. A broad array of pharmacodynamic measures was collected, and multiple blood and urine samples were collected to capture the pharmacokinetic profile of both drugs.
Results: Quinine produced a peak plasma concentration of 488 ng/mL with a Tmax of 1.6h. After 4 consecutive days of once daily dosing, quinine was detectable (144 ng/mL) in plasma 24 hours after the last dose. Estimates suggest a plasma half-life of 8h. In urine, quinine reached a Cmax of 8032 ng/mL with a Tmax of 7.8 h. Urinary accumulation occurred (urine $t_{1/2}$~22h) and quinine was still detectable in urine (464 ng/mL) 72 hours after repeated dosing. Oxycodone did not alter urine or plasma concentrations ($p<.05$), a finding which is supported by the pharmacodynamic data.
Conclusions: The pharmacokinetic profile of quinine in plasma is orderly and appropriate for once daily dosing. Due to its long urinary half-life, quinine may be suitable for urine-based assays to monitor adherence to drugs with similar urinary half-lives or as a tool for detecting multiple missed medication doses.
Financial Support: R01DA016718-08S1 (SLW), UL1RR033173 (UK CTSA)

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GENDER DIFFERENCES IN TRAUMA AND SUBSTANCE USE CHARACTERISTICS AMONG VETERANS WITH PTSD AND SUBSTANCE USE DISORDERS.

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Aims: To examine gender differences in trauma history and substance use disorder (SUD) characteristics among male and female Veterans with current SUDs and co-occurring post-traumatic stress disorder (PTSD).
Methods: Participants (N=93; 82 males, 11 females) met DSM-IV-TR criteria for current SUD and PTSD, and were recruited from the community. The majority (73.6%) served in recent conflicts in Iraq and Afghanistan. Participants completed a battery of assessments, including the Addiction Severity Index-Lite, Timeline Follow-Back, MINI International Neuropsychiatry Inventory, Clinician Administered PTSD Scale, and Beck Depression Inventory.
Results: One-way ANOVA and chi-square tests were used to examine gender differences. In comparison to men, women were significantly less likely to report a history of substance abuse treatment (27.3% vs. 63.4, p=.02). Rates of prior mental health treatment (81.8% vs. 64.6%) and chronic pain treatment (54.5% vs. 61.0%) were statistically equivalent. More women than men endorsed a history of physical abuse (77.8% vs. 30.1%, p<.01) and sexual trauma (72.7% vs. 14.7%, p <.00), while more men endorsed exposure to combat or war zone trauma (94.3% vs. 81.8%, p=.04). Significant differences in the "index trauma" (i.e., trauma associated with the most PTSD symptoms) were revealed with men reporting a military-related trauma and women reporting a sexual assault trauma (p=.03). No significant gender differences in CAPS or BDI scores were revealed.
Conclusions: Although preliminary, the findings revealed gender differences in substance abuse treatment history, as well as trauma history among Veterans with SUDs and PTSD. The findings may be useful with regard to gender-sensitive prevention and intervention efforts. Data collection is ongoing and the full data set would be presented.
Financial Support: NIDA Grant R01 DA030143 (SEB)

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OVERDOSE EDUCATION AND NALOXONE RESCUE KITS FOR FAMILY MEMBERS OF OPIOID USERS: CHARACTERISTICS, MOTIVATIONS AND NALOXONE USE.

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Aims: In response to the overdose epidemic, some support groups for family members of opioid users are providing overdose education and naloxone rescue kits (OEN) to attendees. We describe characteristics, motivations, and naloxone rescue kit use among support group attendees.
Methods: We conducted a cross sectional, multisite study to survey attendees of community support groups for family members of opioid users where OEN training was offered. We developed a 42 item self-administered survey that included demographics, relationship to opioid user, experience with overdose, motivations to receive OEN, and naloxone rescue kit use. We calculated descriptive statistics and compared those who received a naloxone rescue kit to those who did not using chi-square or Fisher's exact tests as appropriate.
Results: Of 126 surveys completed at 8 sites, 99 attendees (79%) had received OEN training and 27 (21%) had not. The trainees were more likely to be parents (85% v 62%, p <0.01), provide financial support (58% v 30%, p <0.01), utilize court-mandated treatment (41% v 15%, p< .01) and to have witnessed an overdose (35% v 12%, p<0.05). The major motivations to receive training were: wanting a kit in case of overdose in their home (67%), encouragement at the beginning of support group meeting (56%) and having heard about benefits (50%). Nine (9%) used a naloxone kit to rescue a family member.
Conclusions: Most family member support groups attendees received OEN training, motivated by wanting to be prepared in case of an overdose, peer encouragement and prior knowledge of naloxone. Several had used naloxone to rescue family members who overdosed. Further study is warranted to understand how best to train family members and the role family training can play in addressing the opioid overdose epidemic.
Financial Support: R25DA03211

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AVOIDING TREATMENT DUE TO FEARS OF VIOLENCE: THE FIRST REPORT OF GENDER-BASED AND INTIMATE PARTNER VIOLENCE IN THE COMMUNITY AND IN THE HOSPITAL AMONG FEMALE HEROIN USERS IN DAR ES SALAAM, TANZANIA.

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Aims: The high HIV prevalence among female drug users in Dar es Salaam contrasts strikingly with their low enrollment in HIV risk reduction services such as methadone assisted therapy (MAT). This study was conducted to examine reasons for this disparity and the role that gender based violence might have in contributing to it.
Methods: We conducted a case-controlled study of female drug users with cases being female heroin users not on MAT and controls being females enrolled in MAT. All patients underwent a structured interview to identify barriers to treatment, including gender-based violence, intimate partner violence (IPV), risky sexual behaviors, and harassment in clinical settings. We fitted logistical binomial regressions within each barrier category with the odds of seeking MAT as the response variable. The unadjusted significant variables were incorporated in a logistical binomial regression and adjusted for demographic and socio-economic determinants of access to healthcare.
Results: We interviewed 296 respondents of whom 202 were not enrolled and 93 were enrolled in MAT services. Our analysis indicated that the likelihood of seeking MAT decreased with increased reporting of discrimination by a healthcare provider (OR=0.11, 95%CI=0.030, 0.298), having a partner who also uses drugs (OR=0.05, 95%CI=0.0197, 0.232) and being in a violent relationship (OR= 0.23, 95%CI=0.108, 0.398).
Conclusions: The findings from our research highlight violence and discrimination as strongly associated with low access to MAT. Ongoing work is needed to address gender-based violence in the community and in healthcare settings. Such work may include the creation of more supportive environments for women to seek MAT (e.g., specific hours for women to access MAT), specific therapy groups, and partner-oriented services.
Financial Support: Yale University

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IS VOLUNTARY HOUSEHOLD SMOKING BAN DIFFERENTIALLY EFFECTIVE FOR MEN'S AND WOMEN'S SMOKELESS TOBACCO USE AND ADDICTION? FINDINGS FROM THE GLOBAL ADULT TOBACCO SURVEY IN INDIA.

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Aims: Smokeless tobacco use has been a chronic problem in South Asia and gender as well as rural-urban disparities may be increasing. Voluntary household smoking bans are a widely advocated public health strategy but their differential effectiveness on smokeless tobacco use and addiction burden among men and women (because of varying gender empowerment norms) are understudied.
Methods: We used data from the Global Adult Tobacco Survey (GATS), a nationally representative survey utilizing globalized standardized methodology conducted in 2009-10 (N=69,296). Voluntary household smoking ban was measured by one item which indicated whether or not smoking was allowed in all areas of the home. Use was defined as use of smokeless tobacco in the past year. Probable addiction was defined as self-reported use of smokeless tobacco within thirty minutes of waking up. We examined the prevalence of smokeless tobacco use and probable addiction (only among current smokeless tobacco users), stratified by gender. Bivariate and adjusted (for smoking status, tobacco exposure, region, past use, education, occupation, wealth) logistic regression analysis were used to examine associations between household ban and use/addiction and differences by urban-rural location.
Results: The prevalence of smokeless tobacco use was 37% and 21% respectively for men and women in rural areas. In urban areas, this corresponded with 24% for men and 11% for women. Among both men and women, over 40% of users were considered probably addicted. Men were more likely to report a ban in both rural and urban areas. In adjusted regressions, household smoking ban significantly reduced smokeless tobacco use and addiction for women. For men, household ban was effective only in urban settings.
Conclusions: Additional research is needed to examine refined regional variations and gender differences between different types of tobacco use and exposure and why voluntary ban is effective for smokeless tobacco control only in certain situations.
Financial Support: NIDA T32DA007313

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A RE-ENGINEERED ANTICOCAINE MONOCLONAL ANTIBODY: DETERMINING H2E2 THERMOSTABILITY AND THERMODYNAMICS OF LIGAND BINDING.

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Aims: The murine hybridoma cell-produced chimeric anticocaine mAb 2E2 (human γ1 heavy, murine λ light chain) was re-engineered as a CHO-cell produced recombinant biologic h2E2 and further humanized by replacing the murine λ chain constant region with human λc sequences. The aims of this work have been to determine its thermal stability and the thermodynamics of ligand binding.
Methods: Capillary differential scanning calorimetry (DSC) measurements have detailed the pattern of thermal-induced unfolding of h2E2 structural domains. Isothermal titration calorimetry (ITC) was used to determine the thermodynamics of ligand binding.
Results: We report that h2E2 has temperature and pH dependent patterns of unfolding stability that are comparable to that of the control murine anticocaine mAb 1BB835. Further, upon binding of the cocaine analog RTI-113 the peak value temperature (Tm) for unfolding of the h2E2 Fab domain increased from 71oC to 79oC and the heat capacity (Cp max) increased 1.8-fold. ITC studies generated Kd values for cocaine, cocaethylene and RTI-113 binding that were comparable to those obtained using radioligand binding. The Gibbs free energy (ΔG) values of binding (approx. -11.0 kcal/mol) for the three ligands were similar but their entropy (tΔS) values indicated differences in their mechanisms of binding.
Conclusions: As no pharmacological agent has yet proven safe and effective as a treatment for cocaine abuse relapse several research groups are currently determining the potential of anticocaine antibodies as immunotherapeutics. A successfully manufactured biologic will require that it maintains stability throughout production, purification, formulation, storage and use. These studies have shown recombinant h2E2 to have the cocaine affinity, temperature and pH structural stability that indicates its suitability for continued clinical development.
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LOW STRIATAL DOPAMINE D2/3 RECEPTOR AVAILABILITY PREDICTS STEEPER DELAY DISCOUNTING IN METHAMPHETAMINE ABUSERS.

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Aims: Drug addicts typically exhibit an abnormally strong preference smaller, immediate over larger, delayed rewards, and this bias undermines their ability to remain abstinent. This propensity to discount delayed rewards may at least partly derive from deficient dopamine (DA) signaling in the striatum, but few studies have attempted to assess this possible link. This study aimed to determine whether discounting of delayed rewards is negatively related to striatal D2/3 receptor availability in methamphetamine (MA) abusers and non-users.
Methods: Healthy adult volunteers (N=59: n=28 MA-dependent, n=31 controls) performed a laboratory test of temporal discounting of financial rewards (delay discounting task; DDT) and underwent PET scans with [18F]fallypride to measure D2/3 receptor availability (indexed by binding potential, BPND). Correlational analyses tested potential relationships between DDT performance and striatal BPND, and explored the possibility of correlations in extrastriatal regions.
Results: MA abusers discounted delayed rewards more steeply, and displayed lower striatal D2/3 BPND than controls. Steeper discounting was associated with lower striatal BPND in MA abusers, but not in controls. Exploratory analyses revealed similar correlations in various extrastriatal regions of MA abusers.
Conclusions: These results provide direct empirical evidence that low D2/3 receptor availability, particularly in the striatum, is associated with an increased bias towards immediate, over delayed rewards. This mechanism appears to be especially exploited among chronic MA abusers, and may help to explain why drug addicts irrationally chose to continue using drugs despite their future negative consequences.
Financial Support: NIDA R01 DA020726; T32 DA024635.

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ACUTE STRESS RESPONSE IN MARIJUANA SMOKERS AND RELAPSE TO MARIJUANA IN THE HUMAN LABORATORY.

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Aims: A single clinical study has shown that among treatment-seeking cocaine users, neuroendocrine response to a stressful personal narrative predicted the severity of cocaine relapse. In this study, we evaluated response to stress in marijuana (MJ) smokers prior to their participation in a human laboratory model of MJ withdrawal and relapse.
Methods: Healthy, non-treatment-seeking daily MJ smokers with no current Axis 1 diagnoses (except MJ dependence) completed the Trier Social Stress Task (TSST), a standardized laboratory stressor involving public speaking and a mental arithmetic task. All had gone at least several hours without MJ prior to the TSST. Stress response was assessed with heart rate, salivary cortisol, and subjective anxiety (State-Trait Anxiety Inventory; STAI). Participants then completed an 8-day inpatient study phase. On day one they smoked experimenter-administered active MJ (5.6%THC), followed by three days in which they could self-administer placebo MJ (0.0%THC). During the final four days, active MJ (5.6%THC) could be purchased using study earnings for self-administration (up to 18 MJ puffs per day). Relapse was defined as active MJ self-administration the first day following abstinence. Data were analyzed for significant differences in stress response between participants who relapsed to marijuana (n=27) and those who did not (n=19).
Results: Data collection is ongoing. Preliminary findings show that the TSST significantly increased both heart rate ($p < 0.05$) and STAI anxiety scores ($p < 0.05$) but did not significantly increase cortisol levels relative to baseline. To date, stress response is not significantly different between participants who relapsed to MJ use versus those who did not. There was no correlation between the severity of MJ relapse (puffs smoked) and cortisol levels.
Conclusions: Although stress responding has been shown to predict severity of cocaine relapse, our preliminary evidence does not suggest that stress responding predicts relapse to MJ or the severity of relapse as measured in the human laboratory.
Financial Support: DA09236, DA19239

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TOBACCO-RELATED MORTALITY AMONG PERSONS WITH MENTAL HEALTH AND SUBSTANCE ABUSE PROBLEMS.

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Aims: The rate of cigarette smoking is greater among persons with mental health and/or substance abuse problems. There is some evidence that persons with mental health and/or substance abuse problems are more likely to die from tobacco-related deaths than from other causes. However, there are few population-based datasets with which to study this relationship.
Methods: The Oregon Health Authority identified persons who received publicly-funded mental health or substance abuse services from January 1996 through December 2005. These cases were identified as having received mental health services, substance abuse services, or both types of services. These cases were then matched to Oregon Vital Statistics records for all deaths (N= 148,761) in the period 1999-2005.
Results: The rate of tobacco-related death rates was higher among persons with substance abuse problems only (53.6%) and those with both substance abuse and mental health problems (46.8%), in comparison to the general population. The rate of tobacco-related deaths among persons with mental health problems only (29.9%) was similar to that in the general population (30.6%). Persons with substance abuse problems only, and substance abuse and mental problems, also died prematurely from tobacco-related deaths; while there were no differences in tobacco-related premature deaths between persons with mental health problems only and the general population.
Conclusions: Persons receiving substance abuse treatment in Oregon were more likely to die, and more likely to die prematurely, of tobacco-related causes as compared to the general population.
Financial Support: Frank Bandiera is currently supported by a postdoctoral fellowship in Tobacco Control at UCSF (R25CA113710).

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COCAINE USE IN LATE ADOLESCENCE: IMPACT OF PRENATAL COCAINE EXPOSURE, SEX/GENDER, AND ONGOING CAREGIVER COCAINE USE.

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Aims: 1. To compare cocaine use in prenatally cocaine-exposed (PCE) and non-cocaine-exposed (NCE) late adolescents; 2. To assess for male-female variations in observed differences in cocaine use in PCE vs. NCE late adolescents; and 3. To determine whether ongoing caregiver cocaine use influences cocaine use in PCE vs NCE late adolescents.
Methods: The study sample consists of 368 late adolescents (mean age 19 years; 189 PCE, 179 NCE, 166 males, 202 females) from the Miami Prenatal Cocaine Study longitudinal cohort of urban African American newborns, with maternal report and toxicology assays of PCE. Follow-up cocaine exposure values are from positive toxicology assays of urine and/or hair from the offspring and their primary caregiver at the 18/19 year study visit, since self-report disclosed negligible exposure. Multiple regression analyses provide estimates of variation with alpha set at 0.05.
Results: At follow-up, risk difference models showed 22% of the PCE group vs.13% of the NCE group had recent cocaine exposure by urine and/or hair cocaine exposure assays ($p<0.05$); odds ratio estimation via GLM disclosed a moderately strong PCE prediction to this cocaine outcome with covariates held constant ($p<0.05$), and with no male-female variations in observed relationships. Despite a strongly positive predictive relationship linking PCE and ongoing caregiver cocaine use, the PCE association with late adolescent cocaine exposure was not moderated by ongoing caregiver cocaine use.
Conclusions: In these estimates, PCE predicts excess risk of cocaine exposure in late adolescence for both males and females, with little evidence of moderation by ongoing caregiver cocaine involvement. Adolescent self-report added little to what toxicological assays disclosed.
Financial Support: NIDA & ORWH: P50 DA 024584 (ESB); R01 DA 006556 (ESB); K01 DA 016720 (VHA)

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EVALUATION OF A BRIEF SMOKING CESSATION INTERVENTION FOR INPATIENT SUBSTANCE USERS WITH ELEVATED DEPRESSIVE SYMPTOMS.

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Aims: Individuals with substance use disorders and depressive symptoms have difficulties quitting smoking cigarettes. Few existing treatments reduce disparities in cessation among these individuals. Previous research demonstrates behavioral activation (BA) reduces depressive symptoms in substance users, as well as smoking and depressive symptoms in community smokers. The current study compared Behavioral Activation for Drug Abusing Smokers (BADAS: BA + nicotine replacement therapy + standard CBT-based smoking cessation) to smoking cessation treatment as usual (TAU: nicotine replacement therapy + self-help manual).
Methods: 24 African American smokers with depressive symptoms were recruited from inpatient substance use treatment and were randomized to 5 sessions of BADAS (M age=39.18, 41.7% female) or TAU (M age=40.17, 16.7% female). In BADAS, clients identified their values and scheduled activities based on them; standard CBT for smoking was also administered. Assessments were conducted at baseline, quit day, 2 weeks and 4 weeks post-quit. The Time Line Follow Back assessed self-reported smoking and expired carbon monoxide provided a biological assessment of abstinence. Cox regression and survival analyses were used to examine differences in smoking as a function of treatment.
Results: Participants in BADAS were significantly less likely to relapse during the first week post-quit ($\chi2(1)=4.44$, $p=.035$). Those in TAU had a mean survival time of 14.75 days, which was shorter than those in BADAS, who had a mean survival time of 23.00 days until relapse to smoking ($\chi2(1)=3.59$, $p=.058$). Individuals in TAU were 4 times more likely to relapse than individuals in BADAS ($\chi2(1)=3.37$, $p=.071$, HR=4.0).
Conclusions: This is the first study to demonstrate that targeting depressive symptoms in substance users would improve their smoking cessation outcomes. BADAS significantly reduced participants' likelihood of relapsing to smoking during the first week post-quit; larger scaled studies are necessary to determine its effects on other outcomes.
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DEVELOPMENTAL HERITABILITY OF INTERNALIZING SYMPTOMS AND CIGARETTE USE CO-OCCURRENCE.

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Aims: Previous research with adult twins has indicated that additive genetic factors contribute substantially to the association between adult internalizing symptoms and cigarette use. This study was conducted to examine how the contribution of genetic and shared environmental factors to the co-occurrence between internalizing symptoms and cigarette use among adolescent twins change during adolescence.
Methods: Adolescent twin pairs (n=1,258) came from the population-based Virginia Twin Study of Adolescent Behavioral Development. Age-specific bivariate twin modeling was performed of the highest number of cigarettes smoked and a composite measure of anxious and depressive symptoms from the Child and Adolescent Psychiatric Assessment. Saturated bivariate Cholesky models for two age groups (14- to 15-, and 16- to 17-year-olds) were compared to reduced models where additive genetic and shared environmental influences were systematically removed and the fit of the nested models compared using OpenMx.
Results: Compared to the saturated bivariate Cholesky, including three sources of genetic variance, a model dropping shared environmental effects caused a reduction in model fit for both groups (x2(3, n=582)=10.73, p<.01; x2(3, n=676)=, p<.01). The best fitting models indicated that 40.9% (for 14 to 15-y-o) and 37.5% (for 16- to 17-y-o) of the total variance was explained by shared environmental factors common to both cigarette use and internalizing symptoms.
Conclusions: The co-occurrence between internalizing symptoms and cigarette use among a sample of adolescent twins appears to result from decreasing shared environmental factors that influence the risk to both traits.
Financial Support: Funding for Dr. Bares' work comes from Dr. James Anthony's R25 DA030310. Funding for the Virginia Twin Study of Adolescent Behavioral Development comes from the following NIH grant, MH-45268.

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HOW IMPORTANT ARE COUNSELOR AND CLIENT CHARACTERISTICS IN DETERMINING OVERALL CLIENT SATISFACTION WITH 12-STEP FOCUSED COMMUNITY COUNSELING GROUPS?

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Aims: Research indicates that client satisfaction at end of treatment is associated with successful treatment outcomes. The present study examines client satisfaction in community counseling groups and counselor and client characteristics associated with increased satisfaction.
Methods: In a pre-intervention phase of a large, multi-phase, multi-site clinical trial, 80 counselors completed a background form and agreed to run five group sessions on 12-step facilitation (12SF) topics, with minimal training and covering the content to the best of their current knowledge and ability. 700 clients in the counselors' groups also agreed to participate and completed a background form prior to attending groups. After the fifth session, clients rated their satisfaction with the 12SF groups on both general and 12SF specific items.
Results: Binary logistic regression for general satisfaction showed that clients under judicial pressure to be in treatment were 46.3% less likely to be very satisfied (OR=.573, p=.003), whereas clients whose counselors had more years of experience were more likely to be very satisfied (OR=1.04, p=.007). For 12S specific satisfaction, clients under judicial pressure were 44.9% less likely to be very satisfied (OR=.551, p=.000) and clients who had counselors that identified as being in recovery were 80% more likely to be very satisfied (OR=1.80, p=.037).
Conclusions: These results suggest that certain client and counselor characteristics are associated with client satisfaction with group counseling, and thus could influence client outcome. Treatment providers may need to 1) develop different strategies to foster higher satisfaction among criminal justice populations, and 2) focus on providing additional training on 12SF to less experienced counselors or those not in recovery in order to increase satisfaction.
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SUBSTANCE USE AND MENTAL HEALTH CONSEQUENCES OF CHILDHOOD TRAUMA: AN EPIDEMIOLOGICAL INVESTIGATION.

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Aims: Exposure to childhood trauma (CT) can have very serious and enduring effects including the development of mental health disorders. Few studies, however, have examined associations between CT and mental health disorders in the general population. The aim of this epidemiological study is to identify the substance use and mental health consequences of CT using data collected as part of the 2007 Australian National Survey of Mental Health and Wellbeing (NSMHWB).
Methods: The 2007 NSMHWB was a nationally representative survey of 8,841 adult Australians. CT exposure and lifetime DSM-IV substance use and mental health disorders were assessed using the World Mental Health Composite International Diagnostic Interview. Analyses were weighted to provide population estimates.
Results: 41% of Australian adults were exposed to a traumatic event during their childhood (before 17 years of age) and 20% experienced their first trauma prior to 9 years of age. The most common CTs were sexual assault, witnessing serious injury or death, and the unexpected death of a loved one. Half of those who experienced CT (53%) met DSM-IV criteria for a lifetime mood, anxiety or substance use disorder (compared to 24% of those who never experienced trauma). The most commonly experienced disorders were alcohol use disorder (29%), major depressive disorder (21%) and PTSD (13%). After controlling for demographic characteristics, the odds of meeting criteria for a mental health disorder were 3.6 times higher among those exposed to CT compared to those who never experienced trauma.
Conclusions: This is the first epidemiological investigation of substance use and mental health consequences of CT in the Australian general population. Exposure to CT is common and puts individuals at risk of developing serious psychological illness. These findings underscore the importance of early intervention for individuals who have been exposed to trauma during childhood.
Financial Support: This research received no financial support. The NSMHWB was funded by the Australian Government Department of Health and Ageing.

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THE CHALLENGING EXPERIENCE QUESTIONNAIRE: CHARACTERIZATION OF ACUTE ADVERSE REACTIONS TO PSILOCYBIN.

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Aims: Acute adverse psychological reactions ("bad trips") to classic hallucinogens (such as psilocybin and LSD), while usually benign with proper preparation before and support during the time of drug action, remain a clinical concern for human research, and a safety concern for recreational use. Anecdotal and clinical evidence suggests that anxiety, panic, depression, and confusion are potential adverse reactions to classic hallucinogens. We apply psychometric analysis to investigate the profile of challenging experiences with psychedelics, and relate this profile to ratings of the overall impact of the experiences.
Methods: We analyzed responses (N=1853) to an online survey study of "bad trips" with psilocybin, and used exploratory and confirmatory factor analysis of stratified subsamples to construct and validate a Challenging Experience Questionnaire (CEQ) from responses to items from the Hallucinogen Rating Scale (HRS), the States of Consciousness Questionnaire (SOCQ), and the 5-Dimensional Altered States of Consciousness questionnaire (5DASC).
Results: Scores from 29 items of the HRS, SOCQ, and 5DASC loaded onto a 6 factors of the CEQ (grief, fear, death, insanity, isolation, and physical distress). These factors differentially predicted the rated difficulty, meaningfulness, spiritual significance, and change in well-being attributed to the challenging effects.
Conclusions: Scores on CEQ factors form a phenomenological profile of challenging experiences with psilocybin, and may provide a framework within which to investigate predictors and persisting effects of these experiences.
Financial Support: This work was supported in part by NIH grants T32DA007209 and R01DA003889, and a grant from the Heffter Research Institute.

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WILLINGNESS TO ENTER DRUG TREATMENT: THE ROLE OF TREATMENT MODELS, COPAYS AND FINANCIAL INCENTIVES.

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Aims: The low proportion of individuals with drug use disorders (DUD) who receive treatment has led to the consideration of alternative treatment models, in addition to addiction treatment center-based care (ATC), to attract patients. These include primary care (PC), and primary care/collaborative care (PC/CC). In addition, out-of-pocket copays and financial incentives may impact willingness to enter treatment. We sought to assess the willingness of out-of-treatment individuals with DUD to enter various drug treatment models and their responsiveness to copays and financial incentives.
Methods: We conducted a nationally representative randomized internet-based survey experiment of individuals screening positive for DUD. Respondents not in treatment were randomized to receive one of 3 treatment vignettes describing key components of ATC, PC or PC/CC. Outcomes included willingness to enter treatment based on treatment model, copays (re-randomized) and, for those not willing to enter treatment, whether financial incentives increased respondents' willingness to enter treatment.
Results: Of 231 respondents with DUD, 26% indicated willingness to enter treatment when it was described as ATC, 42% when described as PC, and 37% when described as PC/CC; p =.04 for ATC vs. PC. Among respondents expressing willingness to enter treatment without a copay, a smaller proportion would enter treatment when each visit incurred a copay: $10 copay (84%); $30 copay (48%); $50 copay (20%). Of the 154 DUD respondents not willing to enter treatment, 62% indicated they did not feel the need for treatment. The percentage of respondents originally unwilling to enter treatment the size of the financial incentive offered per visit impacted willingness to enter treatment: $5 incentive (15%); $10 incentive (23%); $15 incentive (34%); $20 incentive (28%); $25 incentive (29%).
Conclusions: Treatment models, copays and financial incentives should be considered when designing strategies to address willingness to enter drug treatment.
Financial Support: R01 DA 026414

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COGNITIVE-BEHAVIORAL THERAPY AND EDUCATIONAL COUNSELING FOR CHRONIC PAIN AND OPIOID DEPENDENCE.

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Aims: To examine the efficacy of cognitive behavioral therapy (CBT) and educational counseling (EC)—the educational component of CBT augmented by additional psychoeducation on chronic pain and addiction—for co-occurring chronic low-back pain and opioid dependence (POD).
Methods: 90 POD patients received a standard protocol of buprenorphine/naloxone (BUP/NLX) and were assigned to: physician management (PM) alone, consisting of six 10-15 minute medically-focused sessions; PM plus psychologist-delivered CBT (10 sessions over 12 weeks); or PM plus nurse-delivered EC (10 sessions over 12 weeks). Primary outcomes were pain interference, pain intensity, and percentage of opioid-negative urines.
Results: The majority were men (68%), Caucasian (89%), and never married (60%). Completion rates (>90%) and PM attendance (mean of 5.6 of 6 planned sessions) did not vary across conditions. There was a significant overall decrease in average pain interference from 4.6 at baseline to 3.4 at month 3 ($p<.05$) and a significant interaction between condition and time ($p<.05$), favoring PM plus CBT or EC over PM alone: The mean (SD) reductions in pain interference (scored on 0-10 scales) in the CBT, EC, and PM alone groups were 1.7 (1.7), 1.4 (1.6), and 0.6 (1.6), respectively. Pain intensity decreased over time ($p<.05$) but did not differ by group nor was there a significant interaction with group by time. Overall, the proportion of urine samples indicating nonmedical opioid use decreased from 100% at baseline to 31% (95% CI 23%-40%) at month 1, 36% (95% CI 27%-46%) at month 2, and 39% (95% CI 30%-50%) at month 3. Covarying for nonmedical opioid use during BUP/NLX induction, there was a significant interaction between counseling and time ($p<.05$): reductions from baseline were sustained in both CBT and EC groups, while nonmedical opioid use increased in the PM alone group.
Conclusions: Our findings support the efficacy of PM enhanced by CBT or EC for patients with POD treated with BUP/NLX.
Financial Support: NIDA: K23 DA024050, K24 DA00445, and R01 DA024695

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SIGNIFICANTLY LOWER PREVALENCE OF PSYCHOPATHOLOGY IN ASIAN COMPARED TO NON-ASIAN METHADONE MAINTAINED PATIENTS.

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Aims: Comorbid psychiatric illness may affect up to 50% of methadone maintained patients. Previous work has not found significant differences in prevalence of psychiatric illness between Caucasian, Hispanic, and African American methadone maintained patients. Little is known about the prevalence of psychopathology in Asian methadone maintained patients.
Methods: Hmong and non-Hmong subjects who had been on methadone for at least 2 months were recruited from a single urban methadone clinic. Those who were pregnant, had end stage liver disease, or were taking medications known to interact with methadone were excluded. To determine Axis I psychiatric diagnoses, a trained masters level interviewer completed the Structured Clinical Interview for DSM-IV and subjects also completed the Symptom Checklist-90 (SCL-90) to assess levels of psychopathology. Descriptive statistics using chi-square for categorical variables, t-tests and analysis of variance for continuous variables evaluated differences between ethnicities.
Results: 206 subjects mean age 47.2 years (61.7% male) participated. Ethnic distribution was 30.6% Caucasian, 21.4% African American, 9.2% American Indian, Hmong 36.9%. The Hmong were significantly older (56.6 years) and more likely to be male (71.1%). SCL-90 global severity did not differ between groups and methadone dose did not differ between those with normal versus borderline and abnormal scores. The Hmong had more somatization but less interpersonal sensitivity, depression, and paranoid ideation than non-Hmong. Overall the Hmong were less likely to have a DSM-IV diagnosis than non-Hmong (67% versus 29% without). Of those with diagnoses, there was a significantly lower prevalence of anxiety and mood disorder diagnoses but no difference in substance use disorder diagnoses.
Conclusions: Asian methadone maintained subjects have a significantly lower prevalence of DSM-IV axis I diagnoses than non-Asian subjects. We have previously documented superior methadone treatment outcome in Hmong, whether this is influenced by the reduced prevalence in comorbid psychiatric illness remains unknown.
Financial Support: NIH-NIDA K23 DA024663

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OVEREXPRESSION OF MIR-495 IN NUCLEUS ACCUMBENS ATTENUATES COCAINE INTAKE ON A PROGRESSIVE RATIO SCHEDULE OF REINFORCEMENT.

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Aims: MicroRNAs regulate translation of multiple functionally-related genes. We found that the microRNA, miR-495, has several predicted target genes in the Knowledgebase of Addiction-Related Genes database (http://karg.cbi.pku.edu.cn) and is downregulated in the nucleus accumbens (NAc) by acute cocaine administration. Using a lentiviral vector (LV-miR-495) to increase miR-495 expression in the NAc in drug naïve rats, we found an increase in miR-495 and a corresponding decrease in several predicted targets compared to LV-GFP controls, suggesting that these genes are regulated by miR-495 in vivo. In this study, we tested the effects of increasing miR-495 expression on cocaine self-administration (SA).
Methods: Rats were initially trained to self-administer cocaine (0.75 mg/kg/0.1 ml) on a fixed ratio (FR) 5 schedule of reinforcement and then were trained to self-administer 4 different doses of cocaine each available for 30 min within a given session with a 10 min time out between doses. Once stable cocaine SA dose-response functions were established, we infused either LV-miR-495 or LV-GFP into the medial NAc. Testing began 4 days later, including both within- and between-session cocaine SA dose-response tests (0, 0.03, 0.1, 0.3, 1.0 mg/kg, IV; FR5) and tests on a progressive ratio (PR) schedule of cocaine reinforcement using two cocaine doses (0.375 & 0.75 mg/kg).
Results: LV-miR-495 slightly altered the dose-response function for cocaine intake on an FR5 in a manner consistent with a right-ward shift, and produced a more pronounced attenuation of response rates and intake at the high cocaine dose on the PR.
Conclusions: Collectively, these findings suggest that miR-495 may regulate expression of genes in the NAc that are involved in motivation for cocaine. Understanding the role of microRNAs in addiction-related changes in gene expression may offer a novel approach to simultaneously normalize a number of genes that are dysregulated in cocaine addicts.
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GENDER DIFFERENCES IN HEPATITIS C RISK BEHAVIORS.

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Aims: Injection drug users (IDUs) comprise 60% of all hepatitis C virus (HCV) cases in the US. While males are more likely to inject drugs, evidence suggests female IDUs engage in more receptive needle-sharing, increasing their vulnerability to HCV. We hypothesized that female IDUs would report more injection risk behaviors over the past 30 days than male IDUs.

Methods: Baseline data from a randomized controlled trial in methadone maintenance treatment (Masson et al., 2013) was used (N= 489). Chi-square tests were used to analyze gender differences for dichotomous variables and t-tests were used for continuous variables.

Results: The sample was 32% female, 53% non-Hispanic white, 30% African American, 30% Hispanic, and the mean age was 45 (SD=10). No significant differences were found between female and male participants in HCV testing history (85% vs. 79%, respectively) or HCV antibody seropositivity (61% vs. 57%). There were significant differences between females and males in sharing needles (17% vs. 10%, respectively, p=0.048), cotton (30% vs. 20%, p=0.037), and rinse water (27% vs. 14%, p=0.002) among participants who reported injecting (n= 133). No significant gender difference was found in sharing cookers. Female participants reported injecting cocaine less frequently (M=0.3, SD=0.9) than males (M=2.0, SD=5.8; t(187)=3.2, p=0.002) as well as heroin combined with cocaine (M=2.0, SD=2.3; M=4.5, SD=5.7; t(50)=2.2, p=0.031). There were no significant differences in reported days of injecting heroin alone or amphetamine alone.

Conclusions: Both female and male IDUs had high HCV seroprevalence. However, males reported more frequent cocaine, and combined heroin and cocaine injecting. More work is needed to explore potential gender differences in HCV risk behaviors. Gender-specific risk-reduction strategies, including education regarding safe injection practices and treatment for cocaine dependence may be beneficial.

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PHARMACOLOGY OF "NEXT GENERATION" SYNTHETIC CATHINONES: THE FUTURE IS NOW.

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Aims: The abuse of synthetic cathinones, or so-called "bath salts", is a growing public health concern. Common constituents of bath salts, including 3,4-methylenedioxypyrovalerone (MDPV) and 4-methylmethcathinone (mephedrone), have been rendered illegal, but new cathinones are being marketed as replacements. The purpose of the present work was to examine the interaction of newly-emerging cathinones with transporters for dopamine (i.e., DAT) and 5-HT (i.e., SERT).

Methods: Derivatives of MDPV included α-pyrrolidinovalerophenone (α-PVP) while derivatives of mephedrone included 4-methylethcathinone (4-MEC) and 4-methylpyrrolidinopropiophenone (4-MePPP). In vitro assays were carried out in rat brain synaptosomes to assess drug-induced effects on transporter-mediated uptake and release. In vivo microdialysis was carried out in n. accumbens of conscious rats to assess drug-induced changes in extracellular dopamine and 5-HT.

Results: MDPV and α-PVP displayed low nM potency as DAT blockers. Mephedrone was a non-selective transporter substrate with releasing ability at DAT (EC50=38 nM) and SERT (EC50=98 nM). 4-MEC had unusual properties, blocking uptake at DAT (IC50=546 nM) while evoking release at SERT (EC50=123 nM). 4-MePPP blocked uptake at DAT (IC50=248 nM). Microdialysis studies showed that MDPV (0.1-0.3 mg/kg, i.v.) and 4-MePPP (1.0-3.0 mg/kg) selectively increase extracellular dopamine, whereas mephedrone and 4-MEC (1.0-3.0 mg/kg, i.v.) elevate dopamine and 5-HT.

Conclusions: Each of the compounds examined displays a unique profile of in vitro transporter activity. Pyrrolidinophenones like MDPV and α-PVP are potent DAT blockers. Increasing the N-alkyl chain length of mephedrone creates compounds with reduced releasing activity, converting them to DAT blockers. In vivo findings demonstrate that all of the newer replacement cathinones increase extracellular dopamine in mesolimbic circuits, suggesting that these drugs possess a significant risk for abuse.

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DISSEMINATING INFORMATION TO PSYCHOLOGISTS ON EVIDENCE-BASED PRACTICES TO TREAT SMOKING IN HEALTH PRIORITY POPULATIONS.

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Aims: Smoking is the leading cause of preventable death in the U. S. (CDC, 2004). Tobacco use disproportionately impacts health priority populations (http://oas.samhsa.gov).

Although strides have been made in the development of effective smoking interventions, implementing evidence-based interventions into practice continues to be a challenge. Ineffective dissemination of research findings to healthcare providers is a major reason for the low use of evidence-based practices (Brownson, Colditz, & Proctor, 2012).

Psychologists play key roles in smoking research and treatment. The American Psychological Association (APA) Health Disparities Initiative is developing a Best Practices Dissemination Network with the following aims: (1) identify challenges to increasing the involvement of psychology in smoking prevention and treatment with health priority populations and (2) develop strategies to improve dissemination and increase uptake of best practices within psychology. We will describe the needs assessment and evaluation process, program components, barriers, facilitators, and our progress, identifying concerns affecting the extent to which psychologists attend to smoking. They include: Urgency, Awareness, Competency, and Reimbursement. We will describe a research meeting convened with over 80 stakeholders to discuss actions the APA might undertake to strengthen and expand its efforts to prevent and treat tobacco health disparities. Over 130 recommendations were made in six categories: Education/Training; Collaborations; Resources; Research; Advocacy; and Reimbursement. We will describe new activities in each category focusing on the first three and will describe an app developed for professionals

Conclusions: Informed planning of dissemination activities by a trusted source such as a professional association that attends to members' concerns may increase acceptance of evidence-based practices. Some barriers, however, remain difficult to overcome.

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WITHDRAWN

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DOSE AND OTHER FACTORS ASSOCIATED WITH DECREASED PAIN INTENSITY AMONG PATIENTS INITIATING BUPRENORPHINE/NALOXONE.

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Aims: Opioid use disorder (OUD) and pain often co-occur, complicating the treatment of each condition. Owing to its partial agonist properties, buprenorphine/naloxone (BUP/NX) may confer advantages over full agonist opioids for treatment of both conditions. The optimal dose of BUP/NX for comorbid pain is not known. We examined dose and other factors associated with decreased pain intensity among patients initiating BUP/NX for OUD.
Methods: We studied 1171 patients initiating BUP/NX treatment for OUD from 2004-'10. Eligible patients had > 1 pain intensity numerical rating score (NRS) within 30 days before BUP/NX initiation (baseline) and > 1 NRS between 15-90 days after BUP/NX initiation (within treatment). The primary outcome was a clinically-significant NRS decrease (2 or greater) from baseline to within treatment. We used descriptive statistics to summarize baseline characteristics and BUP/NX doses and bivariate measures to assess the relationship between independent variables and change in pain intensity. We used generalized estimating equations to model odds of ≥ 2 NRS decrease, with BUP/NX dose as the independent variable of interest in the subset of patients with a baseline NRS > 2.
Results: The sample was 94% male and 73% white. Mean age was 50. 30% of the sample had PTSD, 63% had major depression, while 44% had alcohol use disorder and 75% had non-opioid substance use disorders. In bivariate analysis, patients without major depression and patients with cancer were more likely to have improved pain intensity with initiation of BUP/NX. In the subset analysis, the following demographic and clinical correlates were associated with a clinically-significant decrease in pain intensity: age 18-29 (compared to 30-39 and 40-49); absence of PTSD and absence of chronic pain. BUP/NX dose was not associated with decreased pain intensity in bivariate or multivariable analysis.
Conclusions: These findings suggest that factors other than BUP/NX dose contribute to improved pain intensity among those initiating it.
Financial Support: VA HSR&D (CDA 08-276); SUD QUERI (SUDQ-LIP1302)

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THE EFFECT OF MARIJUANA COMMERCIALIZATION ON ADOLESCENT POLYSUBSTANCE USE AND TREATMENT.

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Aims: To compare differences in polysubstance use among adolescents in substance treatment pre- and post-marijuana commercialization and evaluate the impact of polysubstance use on treatment-related outcomes among adolescents in substance treatment. Hypothesis: Adolescents entering treatment after marijuana commercialization would have greater rates of polysubstance use and poorer drug treatment outcomes.
Methods: 560 adolescents (Mage = 16.54, SD = 1.93), admitted to outpatient substance treatment were treated with weekly, individual, cognitive behavioral therapy sessions. Participants provided urine drug screen (UDS) samples at each weekly appointment, which were sent to a commercial laboratory for quantitative THC, opiate, cocaine, benzodiazepine, alcohol, and amphetamine levels. Participants entering treatment pre- and post-commercialization of marijuana were compared using t-tests, and hazard models were estimated to assess differences in marijuana abstinence across treatment for adolescents with and without polysubstance use.
Results: Compared to adolescents who entered treatment prior to the commercialization of marijuana, adolescents who entered treatment after the commercialization of marijuana had more positive UDSs for non-marijuana illicit substances (t=-2.202, p=0.036), and were more likely to use both cocaine (t= -3.406, p= 0.002) and amphetamines (t=-3.008, p=0.006). Adolescents who only used marijuana were 1.39 times more likely than adolescents who had polysubstance use to have a negative UDS at the end of treatment (CI: 1.02-1.89; p<0.05) and were 1.34 times more likely to have a shorter latency to first negative UDS (CI: 1.03-1.75; p<0.05).
Conclusions: These findings demonstrate that adolescents exhibit more polysubstance use during an outpatient substance use treatment program after marijuana commercialization than before marijuana commercialization and that adolescents with polysubstance use, compared to those with marijuana use alone, had poorer treatment outcomes.
Financial Support: T32 MH15442-36

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EFFECTIVE HIV AND SUBSTANCE ABUSE PREVENTION PROGRAMS FOR AFRICAN-AMERICAN WOMEN: ATTENDING TO CULTURE AND CONTEXT.

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Aims: The goal of this paper is to review risk and protective factors for both drug and HIV risk and culturally informed approaches that reduce risk and increase protective factors among African American women.
Methods: African American women are at much higher risk for HIV than women from other racial and ethnic groups. In 2010, 64% of the new HIV infections among women in the United States were among African American women. Alcohol and other drug use often precede or co-occur with risky sexual behaviors. Programs that simultaneously target both are likely to be more efficacious than those that target one. We review risk and protective factors for both drug and sexual risk and culturally informed approaches that may reduce risk factors and increase protective factors. We first review individual-level and structural risk factors. Some individual-level risk factors include trauma, stress, depression, anxiety, and ego-depletion. Structural-level risk factors include discrimination, unemployment and underemployment, living in a low resource community, negative media images, and lack of preventive health care including mental health care. We next review protective factors that may attenuate individual and structural level risk factors. Some of these include high racial identity, social support networks, community assets, religiosity, and accessible health care. We then review strategies and programs that have addressed drug and sex risk with special attention to culturally specific programs. We discuss our work that has involved adding a drug education/prevention component to culturally specific HIV prevention programs for African American women. Finally, we provide recommendations for how drug prevention information can be added to existing HIV prevention programs while maintain program integrity.
Conclusions: Both drug and HIV risk for African American women can be reduced.
Financial Support: Virginia Commonwealth University

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POST-TRAUMATIC STRESS DISORDER AND CHANGE IN DRUG AND ALCOHOL DEPENDENCE AMONG RECENT VETERANS.

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Aims: As part of an ongoing study on veteran reintegration in New York City, we interviewed 269 recent veterans who separated from the military between 2008-2012 about their mental health, substance use and social adjustment challenges at baseline and conducted follow-up interviews with 242 veterans a year later.
Methods: We analyzed self-reported post-traumatic-stress-disorder (PTSD) symptoms and other selected factors as predictors of change in drug dependence and alcohol dependence between assessments.
Results: In a multiple regression controlling for drug dependence at baseline, higher drug dependence at follow-up was significantly associated with age younger than 30 (Beta = 0.13, t = 2.1, p < 0.05), not being enrolled in school (Beta = 0.14, t = 2.3, p < 0.05), higher PTSD scores at baseline (Beta = 0.25, t = 3.6, p < 0.01), and increase in PTSD symptoms between assessments (Beta = 0.17, t = 2.6, p < 0.05). In a parallel multiple regression controlling for alcohol dependence at baseline, higher alcohol dependence at follow-up was significantly associated higher PTSD scores at baseline (Beta = 0.39, t = 5.5, p < 0.001), and increase in PTSD symptoms between assessments (Beta = 0.34, t = 5.2, p < 0.001), but not age or school enrollment.
Conclusions: Ongoing PTSD symptomology is associated with ongoing drug and alcohol dependence in this veteran population. For drug dependence, older age and engagement in school predicts less drug dependence over time. Our findings suggest that drug and alcohol prevention interventions need to be targeted toward veterans with PTSD, especially younger veterans and those not connected to school.
Financial Support: This research was supported by a grant from the National Institute on Alcohol Abuse and Alcoholism (R01 AA020178).

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CHARACTERIZING INTERPREGNANCY INTERVALS OF OPIOID-MAINTAINED WOMEN.

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Aims: Nearly 90% of pregnancies in opioid-maintained women are unintended, suggesting that the spacing of these pregnancies may be less than optimal. This is a potential concern because interpregnancy intervals that are too short (≤ 18 months) or too long (≥ 59 months) are independently associated with adverse outcomes including preterm birth, small for gestational age, and low birth weight. We examined the reproductive histories of a sample of opioid-maintained women paying particular attention to interpregnancy interval.
Methods: Forty-one women attended an intake assessment for a clinical trial designed to improve contraceptive use among opioid-maintained women who did not want to be pregnant in the next 6 months. Thirty-eight provided information about their reproductive history.
Results: Women averaged 30.3 years of age (range, 21-38). The majority had never been married (64%), had a high school education (74%) and identified as Caucasian (67%). In this sample, the average age at first pregnancy was 18.3 years old (range, 13-29). Women reported an average of 3.6 pregnancies (range, 0-10). Of the 127 pregnancies reported, 107 (84%) were unintended. Although the average interpregnancy interval was 37.1 months, two-thirds of all interpregnancy intervals were higher risk, with 43% categorized as too short (M=15.4 months) and 23% categorized as too long (M= 84.6 months).
Conclusions: Preliminary data indicate that the majority of interpregnancy intervals in this sample of opioid-maintained women were higher risk because they were too short or too long, potentially compounding poor outcomes in this already at-risk group. These findings underscore the importance of providing family planning services to opioid-maintained women.
Financial Support: Supported by R34 DA030534 from the National Institute on Drug Abuse

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HIV-1 TRANSGENIC RAT: ALTERED MOTIVATED BEHAVIOR FOR NATURAL REWARD.

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Aims: Patients with HIV-1 associated neurocognitive disorders (HAND) exhibit changes in the mesocorticolimbic system, and frequently have mood-motivation disturbances. The HIV-1 transgenic (Tg) rat also has mesocorticolimbic alterations, however the internal motivational state of the Tg rat has not been determined. The present study investigates potential deficits in motivated behavior for a natural reward, sucrose, in the Tg rat.
Methods: Ovariectomized Tg (n=14) and control F344 (n=15) rats were trained using a fixed-ratio (FR1) schedule of reinforcement using a 5% (w/v) sucrose solution while water restricted. Animals were trained to respond on two active levers programmed to control for position bias (± 5 consecutive responses on either lever); a back wall lever had no programmed consequences. Following response stabilization daily water restriction ended; a FR1 was used to determine response rates for different concentrations of sucrose solutions (1%, 3%, 5%, 10%, 30%) and water. In order to more directly quantify differences in motivated behavior, a progressive-ratio (PR) schedule of reinforcement was employed using identical sucrose concentrations. Two active levers were available, potential position bias was monitored but not controlled.
Results: There was a significant main effect of genotype; Tg rats responded less than controls in all conditions ($p<.001$). The Tg rat displayed a rightward and downward shift ($p<.001$) in the dose-response curve of earned reinforcers in the FR1 task. Similarly, the PR dose-response curve for active lever presses displayed a rightward and downward shift ($p<.001$).
Conclusions: The Tg rat has a lower internal motivational state for sucrose, a natural reward. These results may be analogous to individuals with HAND and comorbid disruptions in the mood-motivation facet of depression. Modeling the deficits in motivated behavior in HAND, as previously established for the primary neurocognitive impairments in HAND (Moran et al.,2012a, 2012b, 2013), provides a strong foundation to develop efficacious pharmacotherapeutic interventions.
Financial Support: NIH grants DA013137, HD043680, DA021287, GM081740

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EFFECTS OF SEX AND REMIFENTANIL DOSE ON THE ACQUISITION OF RESPONDING FOR A REMIFENTANIL-ASSOCIATED STIMULUS.

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Aims: Conditioned reinforcement by opioid-associated environmental stimuli may contribute to opioid abuse and dependence by controlling responding when drug itself is unavailable. The factors that determine opioid-conditioned reinforcement, however, are not well characterized. The present study assessed the effects of animals' sex and drug dose on the acquisition of responding for a stimulus associated with the μ-opioid agonist, remifentanil.
Methods: First, in Pavlovian conditioning sessions, male and female Sprague-Dawley rats (age > 65 days) were given response-independent IV injections of remifentanil paired with a light-noise compound stimulus. Separate groups of rats received different doses of remifentanil (0.0-32.0 μg/kg/injection); the same light-noise stimulus was used for all rats. Then, in instrumental acquisition sessions, the ability of the stimulus alone to reinforce a new response was tested. All rats were given access to two nose-pokes: active responses produced the light-noise stimulus alone, whereas inactive responses had no scheduled consequences.
Results: In both sexes, acquisition of responding for the stimulus (i.e., active nose-poke > inactive nose-poke) depended on the dose of remifentanil with which the stimulus was paired. Rats did not acquire responding after vehicle-stimulus pairing. Active, but not inactive, responding changed significantly with remifentanil dose. In both sexes, the dose-effect function for active responding was biphasic, with a peak at 10.0 μg/kg/injection. Males and females differed most notably at the highest dose of remifentanil tested: females, but not males, acquired responding for the stimulus after it was paired with 32.0 μg/kg/injection.
Conclusions: Consistent with remifentanil-conditioned reinforcement, both male and female rats learned to make a novel response to produce the stimulus alone after it was paired with an appropriate remifentanil dose. These results may be relevant to the motivational effects of opioid-associated stimuli in opioid-using men and women.
Financial Support: T32DA07268, R01DA020669, R01DA024897, R01DA032943

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RECRUITING FOR AN SMS SMOKING CESSATION INTERVENTION IN PERU: PILOT STUDY RESULTS.

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Aims: For research on mobile phone SMS smoking cessation interventions, we aimed to evaluate paid versus unpaid Facebook recruitment alternatives.
Methods: In an IRB-approved protocol to recruit on 15 Facebook paid ad days (FBPAD) vs 15 unpaid days, a Peru-based Spanish language FB page was design and 125 messages were posted in the Facebook site. We sought pilot study participants who met inclusion criteria: active smoking frequency/intensity, mobile phone & SMS use, & quit readiness.
Results: For the $250 FB ad fee, 63,538 views elicited 3,866 FB page clicks and 250 online respondents, with most (n=208; 83%) responding on FBPAD. 70 met age & smoking frequency/intensity criteria, of whom 40 had quit readiness, had mobile phone, & knew SMS messaging. [Only 23 (9%) resided in Lima.] Final ad cost to this stage was >US$10 per each valid completed survey with all inclusion criteria met and study restriction to Lima residents. For interventions with a national reach, unit cost was <US$7.
Conclusions: For study recruitment, a paid FB ad may be less useful in Peru than in other places, and may be most valuable in Peru when interventions can be designed to have a national reach. Nonetheless, as compared to alternatives for pilot studies, the yield was sufficient. We concluded that our larger-scale randomized trial of SMS texting interventions should use the paid FB ad approach, but we are continuing to experiment with alternative mall-intercept and pedestrian interventions. The option of respondent-driven recruitment has been proposed, but our concern is a resulting interdependence of observations, and resulting study design effects that ultimately might reduce statistical power of the intervention evaluations.

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IMPLANTABLE AND ORAL NALTREXONE FOR PREVENTING RELAPSE IN OPIATE ADDICTS: A PSYCHOMETRIC EVALUATION.

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Aims: Naltrexone is a μ-opioid receptor antagonist that blocks the euphoric effects of heroin and opioids. Opioid craving, depression, anxiety, and anhedonia are triggers for relapse and dropping out of treatment. It is important to evaluate the effect of implantable and oral naltrexone on craving, depression, anxiety and anhedonia.
Methods: 306 patients with opioid dependence were enrolled into three cell (102ss/cell) randomized, double-blind, placebo-controlled, 6 month trial and received implantable ntx, oral ntx (50 mg/day), or placebo. Psychiatric evaluations were performed using the Visual Analog Scale of Craving for opiates, Beck Depression Inventory, Spielberger State-Trait Anxiety Test, and Chapman Scale of Physical and Social Anhedonia. Psychometric variables were analyzed using ANOVA repeated measures with Tukey test for between group post hoc comparisons.
Results: The percentage of patients that completed 6 months of tx without relapse was: 52.9% in the ntx-implant group, 15.7% in oral ntx (survival analysis, log-rank test, P<.001), and 10.8% in the placebo group (P<.001). There was a significant decrease of craving over the course of tx from 3-3.5 on a 10-point scale at baseline to 0.5-1.1 at 6 months among those who were retained in treatment ($F_{5,1095}$= 21.2; $p < 0.001$). Psychiatric symptoms including depression, anxiety, and anhedonia were moderately elevated at baseline and gradually decreased to normal levels within the first 1-2 months among all patients who remained in tx and did not relapse, with no differences between groups.
Conclusions: The improvements in heroin craving, depression, anxiety, and anhedonia among those who were retained in treatment and did not relapse are most likely an effect of treatment success and not specifically related to naltrexone since they occurred regardless of medication group. Long-term blockade of opiate receptors with naltrexone did not induce anhedonia or depression.
Financial Support: National Institute on Drug Abuse (1-R01-DA-017317 and KO5 DA-17009)

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ABUSE POTENTIAL OF ESLICARBAZEPINE ACETATE IN RECREATIONAL SEDATIVE USERS.

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Aims: Eslicarbazepine acetate (ESL) is an antiepileptic drug that is converted to eslicarbazepine after oral administration. Adverse events in Phase I to III studies of dizziness and somnolence suggest that ESL has detectable CNS effects in addition to its effects as an anticonvulsant. The purpose of this study was to evaluate the abuse potential of ESL compared to alprazolam (ALZ) and placebo (PBO) in recreational sedative users.
Methods: This was a randomized, double-blind, PBO- and active-controlled crossover study. Healthy recreational sedative users (N=44) received single oral doses of ESL (800 mg, 1600 mg, 2000 mg, and 2400 mg), ALZ (1.5 mg and 3.0 mg) and PBO. Eligible subjects passed a qualification session to ensure they could distinguish and show positive effects of 2 mg ALZ. In the main study, subjective measures (eg, VASs and ARCI) were evaluated up to 24 hours postdose. Pharmacokinetic (PK) samples were also collected over 24 hours postdose at pre-specified timepoints.
Results: Mean peak Drug Liking was significantly higher for both doses of ALZ compared to PBO ($p<0.05$), confirming the validity of the study. All doses of ESL demonstrated significantly lower Emax on Drug Liking compared to both ALZ doses ($p < 0.0001$). The peak Drug Liking score for 800 mg ESL (therapeutic dose) was similar to PBO ($p = 0.19$). At the 3 supratherapeutic doses (1600-2400 mg), ESL showed statistically greater Drug Liking compared to PBO; however, the magnitude of the effect was minimal (mean difference range= 9.3 - 13.3 out of 100). ESL also showed significantly lower effects compared to ALZ on most secondary subjective measures. In this study single doses of ESL up to 2400mg were relatively well tolerated.
Conclusions: ESL effects were significantly lower than ALZ on Drug Liking VAS and the majority of secondary endpoints, including assessments of positive and sedative effects. In this study single doses of ESL demonstrated no evidence of abuse potential in recreational sedative users.
Financial Support: The study was funded by Sunovion Pharmaceuticals Inc.

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FACTORS ASSOCIATED WITH PRECURSORS TO INITIATING OTHER PEOPLE INTO INJECTION DRUG USE.

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Aims: Most people are initiated into drug injection by a person who injects drugs (PWID). To develop interventions for preventing PWIDs from initiating others into drug injection, we need more information about precursors to initiating others. Based on Stillwell et al., 2005 and Strike et al., 2010, precursors to initiating others into injection include injecting in front of non-PWID, describing how to inject to non-PWIDs, and self-reported likelihood of initiating someone. Our aim was to examine factors associated with precursors to initiating others into drug injection.
Methods: Interviews with PWID (N=605) were conducted in California during 2011-2013. Interviews included items on demographics, drug use and drug injection initiation. Precursor variables were transformed into a composite score which, based on statistical diagnostics, was further refined into a dichotomized variable; those who endorsed two or three precursors were classified as 'yes' and those who endorsed one or zero were classified as 'no'.
Results: In multivariate logistic regression analysis, the following variables were associated with >two precursors: obtaining syringes from an unauthorized source (Adjusted Odds Ratio [AOR]=2.59; 95% Confidence Interval [CI]=1.73, 3.90), being born in the eighties or later (AOR=2.49; 95% CI= 1.43, 4.35), injecting in a public location (2.12; 95% CI=1.40, 3.23), injecting other people (AOR=1.92; 95% CI= 1.26, 2.94) and having a steady sex partner who is a PWID (AOR=1.78; 95% CI=1.16, 2.73).
Conclusions: Reducing initiation of non-PWIDs into injection drug use is an important goal for reducing drug-related harms. Intervention development to prevent injection initiation should start with a focus on risk environment variables such as public injection and unauthorized source of syringes. In addition, interventions should address relevant behavioral and demographic characteristics such as younger PWID, those in sexual relationships with PWIDs, and people who inject others.
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IEPI. EPIDEMIOLOGY OF ONE.

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Aims: 1. To introduce a concept of individual epidemiology
2. To illustrate how epidemiological methods could be used to analyze intensive data within a single individual
Methods: Data:
We used daily drinking records from 30 subjects who reporting their alcohol consumption as well as evaluations of the mood and levels of stress.
We have also used simulated daily data based on theoretical models and ethnographic data of heroin use and smoking
Analysis methods:
We applied traditional epidemiological methods to intensive data from drug and alcohol using individuals. Specific methods used were: pattern recognition, Markov models, regression analysis, and piece-wise reinforced learning models.
Results: We showed similarity between the features of infectious disease epidemiology and the features of individual drug use patterns. We have considered individual epidemics in daily drinking, identified patterns and pattern shifts, and applied modeling techniques to predict future drug use. Specifically, we have identified 8 patterns of drinking behavior and shifts between these patterns that could represent within-individual "epidemics". We illustrated the existence of different regimes of drug use that are analogous to endemic and epidemic states in traditional epidemiology.
Conclusions: We present novel approaches to the analysis of intensive data collected within one individual. While technological advantages of social media and mobile technology open new opportunities in collecting intensive behavioral and drug-using data within one individual, traditional epidemiological mindset demand generalizability to a larger population. We argue that a single individual could be viewed as an entire population of drug using and behavioral events. We show how traditional epidemiological methods, that are usually applied to populations of humans, could be applicable to a single individual and thus used for self-monitoring and forecasting of epidemic outbreaks within an individual.
Financial Support: R01DA025163 Researching social dynamics of local methamphetamine market
R03AA019755-01 Patterns of Alcohol Consumption
R21DA032670-01

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REPEATED EXPOSURE PRODUCES TOLERANCE TO SOME OF THE ABUSE-RELATED SUBJECTIVE EFFECTS OF ORAL TRAMADOL IN HUMANS.

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Aims: Tolerance develops to many of the behavioral and clinical effects of opioids. Relatively few studies have investigated the development of tolerance to the subjective effects of opioid drugs and no studies have reported tolerance to the subjective effects of tramadol in humans. The purpose of the present investigation was to determine whether tolerance develops to the subjective and physiological effects of tramadol following repeated intermittent exposures. We hypothesized that ratings of positive and abuse-related subjective-effects measures would be decreased with repeated exposures to tramadol.
Methods: Nine (N = 9) sporadic opioid users were administered oral tramadol (100 mg) or placebo across the first six sessions of a larger drug discrimination study and subjective-effects ratings and physiological measures were collected. All participants received tramadol during the first two sessions and received tramadol or placebo twice each during the last four sessions in randomized order. Data were analyzed as peak or trough using separate single factor repeated-measures analysis of variance with Tukey's multiple comparisons. Linear trend analyses were conducted on data from experimental sessions where participants received active tramadol.
Results: Tramadol significantly increased ratings of several abuse-related subjective-effects measures such as Good Effects, Like the Drug, and Willing to Take the Drug Again initially but ratings on these measures gradually declined with repeated administration suggesting the development of tolerance. By contrast, tolerance did not develop to the physiological effects of tramadol (i.e., miosis).
Conclusions: Although further research is needed to elucidate the mechanisms that mediate tolerance to the effects of tramadol, these findings suggest that tolerance may contribute to its limited abuse potential in humans.
Financial Support: The present research was supported by the National Institute on Drug Abuse (R01DA025649 and T32DA035200) of the National Institutes of Health.

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ENERGY DRINK USE BY ADOLESCENTS AND EMERGING ADULTS SEEKING CARE IN THE EMERGENCY DEPARTMENT: ALCOHOL, DRUGS, AND OTHER RISK BEHAVIORS.

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Aims: Consumption of alcohol mixed with energy drinks by young people presents concerns about the effects on perceived intoxication and risk behaviors. Emergency Department (ED) visits due to energy drinks have risen drastically. Among youth with past-year alcohol use who visited an ED, we assessed frequency of consuming alcohol mixed with energy drinks or consuming both on the same occasion (Combined), reasons for and consequences of Combined use, and relationships with drug use and other risk behaviors.
Methods: Youth aged 14-20 completed past-year surveys at the ED visit. Among 439 drinkers, mean age was 18.6 years (SD=1.4), 41% were male and 73% were Caucasian. We grouped patients into those who drank alcohol, but not energy drinks (Non-users; 41%, n=178), those who drank alcohol and energy drinks on separate occasions (Separate; 23%, n=103), and those who Combined (36%, n=158).
Results: In Combined users, consequences included feeling jittery (71%), trouble sleeping (46%), and increased energy followed by a crash (35%). Reasons for combining were: hiding the flavor of alcohol (39%), liking the taste (36%), and staying awake (32%). Combined users had the highest rates of risk behaviors (e.g., drug use, multiple sex partners, sex after drinking, driving after drinking, alcohol use severity [AUDIT]). Multinomial logistic regression indicated that compared to Non-users, Combined users were more likely to be male, have had sex after using alcohol/drugs, have used drugs, and have higher AUDIT scores. Combined users, compared to the Separate users, had significantly higher AUDIT scores. Separate users compared to Non-users were more likely to be male, and had lower AUDIT scores.
Conclusions: Combining energy drinks and alcohol use is a marker for involvement in other risk behaviors among drinking youth. Future longitudinal studies are needed to determine longitudinal relationships of energy drink use on substance use problem trajectories.
Financial Support: NIAAA #018122

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AFFECT AND IMPULSIVITY IN DAILY RISKY BEHAVIOR.

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Aims: Urgency (URG) is an aspect of personality defined as the tendency to engage in impulsive behavior under the condition of strong affect. Emerging research has explored this variety of impulsivity in terms of substance abuse (Kaiser et al., 2012). However, questions remain regarding how URG contributes to emotions in the moment to promote risky behavior. The aim of the current study was to explore how urgency interacts with mood states to predict risky behaviors and substance use.
Methods: Participants were 115 college undergraduates (57% male) who completed a laboratory protocol including the Alcohol Use Disorders Identification Test (AUDIT) and the UPPS measure of impulsivity. Participants were then provided palm pilots for one week to gather information about mood states (e.g., I feel sad) and risky behaviors (e.g., Doing something I might regret, Doing something exciting). Samples were gathered at 90-minute intervals, between the hours of noon and midnight, with a maximum of 64 assessments.
Results: Palm pilot mood data were consolidated and averaged to form a Negative Affect (NA) and a positive affect (PA) variable. These variables were entered simultaneously with Urgency in hierarchical regressions to test main effects and product terms were entered to explore interactive effects. For the variable "Doing something I might regret," there were main effects for both URG and NA, but no interactive effect. For the variable "Doing something exciting," there was a main effect for PA, and there was an interactive effect indicating that the relation between engaging in exciting behavior and PA was stronger for those high in URG. For the AUDIT, there was a main effect for NA, and there were two significant interactive effects indicating that the relation between problematic drinking and strong emotions (PA or NA) is stronger for those high in URG.
Conclusions: These findings suggest that mood states may act as catalysts for the activation of the trait of Urgency, and further indicate that for these individuals, emotional regulation may be a key to prevent future risky behavior and substance use.
Financial Support: NIDA DA005312

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ROLE OF PROJECTIONS FROM VENTRAL SUBICULUM TO NUCLEUS ACCUMBENS SHELL IN CONTEXT-INDUCED REINSTATEMENT OF HEROIN SEEKING.

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Aims: In humans, exposure to contexts previously associated with heroin use can provoke relapse. In rats, exposure to heroin-paired contexts after extinction of drug-reinforced responding in different contexts reinstates heroin seeking. This reinstatement is attenuated by inhibition of glutamate or dopamine transmission in nucleus accumbens shell or inactivation of ventral medial prefrontal cortex (mPFC). Additionally, we demonstrated a causal role for the projections from ventral mPFC to accumbens shell in this reinstatement.
Ventral subiculum also sends glutamatergic projections to accumbens shell, and inactivation of ventral subiculum, but not posterior CA1 subfield of the hippocampus, decreases context-induced reinstatement of heroin seeking. Here, we examine the contribution of glutamatergic projections from ventral subiculum to accumbens shell in this reinstatement using the retrograde tracer Fluoro-Gold (FG).
Methods: Rats were trained to self-administer heroin for 12 days; drug infusions were paired with a discrete tone-light cue. Lever pressing was subsequently extinguished in a non-drug-associated context in the presence of the discrete cue. Rats were then tested in the heroin- or extinction-associated contexts under extinction conditions.
Results: Exposure to the heroin, but not extinction, context reinstated lever pressing. Context-induced reinstatement was associated with increased Fos expression in ventral subiculum neurons, including those projecting to accumbens shell.
Conclusions: Our findings demonstrate that activation of glutamatergic projections from ventral subiculum to accumbens shell promotes heroin relapse. We are currently exploring a causal role for these projections in context-induced reinstatement of heroin seeking.
Financial Support: NIDA/IRP

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THE EFFECT OF HIGH STRESS ON T-CELL PROTEIN EXPRESSION IN CHRONIC DRUG USERS: HIV IMPLICATIONS.

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Aims: Stress and drug use may work in synergy to affect immune response. We aim to (1) group chronic poly drug users (PDU) according to psychological, physiological and immunological characteristics, and(2) examine stress impact on plasma cytokine profile and protein expression of T-lymphocytes from HIV+ and HIV- PDUs.
Methods: In non-PDU HIV-HCV- controls (n=10) and PDU samples (n=47; 20% female, age 18-35 yrs), stress was measured by the PERI and cortisol/DHEA quantification. Cellular immune response has been evaluated by CD4/CD8 quantification. Protein expression alterations were detected through proteomics.
Results: HIV-HCV- (18), HIV+HCV- (7), HIV-HCV+ (13), HIV+HCV+ (9) and non PDU HIV-HCV- control group(10).
PERI scale scores were related to low and high cortisol levels. Immunologically, among 18 HIV-HCV- PDU 100% had > 410 CD4 cell counts/ul; 5 of 7 HIV+HCV- PDU had high CD4 counts; all 10 non-PDU HIV-HCV- had normal CD4 cell counts. The proteomic data identified proteins showing altered expression mainly in oxidative stress, proteolytic and glycolytic enzymes,inhibitors and structural proteins in the group of PDU+ with high stress as compared to those with low stress values.
Conclusions: Our findings allowed the identification of several protein markers candidates for early diagnostic and/or treatment of PDU under stress. Further, the scientific processes implemented to stratify PDU+ and PDU- users according to physiological, immunological and psychological measurements are important to correlate with the protein profile of the participant groups. This will contribute to the deeper understanding of the effect of stress in the PDU and underlying mechanisms for drug of abuse prevention.
Financial Support: Supported by NCRR (5G12RR003035), NIMHHD (8G12MD007583), NIDA (2R24DA013335; R25DA030310).

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EARLY INITIATION OF ALCOHOL AND ILLICIT DRUG USE: ASSOCIATIONS WITH PSYCHOPATHOLOGY AMONG INPATIENT SUBSTANCE USERS.

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Aims: Early initiation of alcohol use (AU) and illicit drug use (DU) has been associated with later psychopathology. However, the majority of research has explored these relations among community samples. This study examined the effect of early initiation of AU and DU on later problems in low-income adults seeking addiction treatment. We hypothesized that early initiation of AU and DU would be associated with increased psychiatric disorders and substance use disorders (SUDs).
Methods: The study recruited 399 consecutive admissions (30.6% female) from a substance use treatment facility. Participants were assessed for past and current psychiatric disorders using the Structured Clinical Interview for the DSM-IV and also reported on age of first alcohol and substance use.
Results: Poisson regression analyses indicated that early initiation of AU was significantly related to more current (B=-.04, p<.001) and past psychiatric disorders (B=-.03, p=.02) and more current (B=-.03, p=.007) and past (B=-.06, p<.001) SUDs. Results also showed that early initiation of DU was significantly related to more current (B=-.03, p=.004) and past (B=-.04, p<.001) SUDs, but not related to the total number of psychiatric disorders. Logistic regression analyses further showed that early age of AU was significantly related to increased psychotic symptoms, anxiety disorders, personality disorders, and SUDs (B's=-.06 to -.23, p's<.05). Considerably fewer relationships were evidenced for early initiation of DU, with early onset predicting only antisocial personality disorder and SUDs (B's=-.01 to -.12, p's<.05).
Conclusions: Our findings suggest that early initiation of AU is strongly related to subsequent psychiatric and SUDs among adults seeking addiction treatment, which is consistent with research targeting community individuals. Yet, the relative lack of findings for DU contrasts the typical findings from research targeting community individuals. Implications of these results for low-income substance users are discussed.
Financial Support: University of Maryland, Department of Psychology

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LONGITUDINAL PREDICTORS OF 12-STEP ATTENDANCE AMONG SUBSTANCE-ABUSING WOMEN.

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Aims: Although 12-step support groups present an easily accessible means of support for individuals with substance use disorders, the program may selectively attract European Americans and those who are already involved with religious activities (Arroyo et al., 2002; Maude-Griffin et al., 1999). Its ability to attract more marginalized groups, such as survival sex workers, is less known. This study tested whether race/ethnicity, attendance in religious activities, sex work, as well as frequency of substance use, predicted 12-step meeting attendance at baseline and 6-months post-baseline among treatment seeking women.
Methods: The sample included 183 treatment seeking substance use disordered women. The data were analyzed by HLM 7 Bernoulli model with EM Laplace-2 estimation. Ethnicity and paid sex at baseline were used to predict the intercept and the time slope of 12-step participation. Percent days of drug use and religious activity attendance were used as time-varying covariates.
Results: 12-step participation did not change from baseline to 6-months. European American women [β = -1.65, S.E. = 0.58, p < 0.01] and those who reported engaging in paid sex [β = 2.54, S.E. = 0.76, p < 0.01] were more likely to attend 12-step programs than their counterparts. Increased involvement in religious activities from baseline to the 6-m follow-up was significantly associated with an increased likelihood of participating in 12-step programs [β = 0.80, S.E. = 0.33, p < 0.05]. An increase in the use of drugs was significantly associated with a lower likelihood of participation in 12-step meetings over time [β = -0.02, S.E. = 0.005, p < 0.01].
Conclusions: Being European-American, and engaging in sex work and religious activities predicted more 12-step attendance. Also, as substance use increased, 12-step attendance decreased. The twelve-step program may be a viable and potentially under-utilized intervention for sex workers. However, more research identifying the barriers to 12-step participation among women of color and those not active in religious activities is needed.
Financial Support: This study was supported by a NIDA grant #R01DA023062 to the 4th author.

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EXPLORATORY INTERVIEWS WITH E-CIGARETTE AND SNUS USERS.

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Aims: To conduct exploratory interviews with e-cigarette and snus users. Emerging themes and constructs will inform qualitative coding for a proof-of-concept study designed to evaluate the feasibility of using Internet forums to understand perceptions, behaviors, and use patterns associated with new tobacco products (NTPs).
Methods: Semi-structured phone interviews were conducted with e-cigarette and snus users to address use of these NTPs (e.g., use history, current use, cessation attempts); perceptions regarding health risks of NTPs versus cigarettes, NRTs, and smoking cessation; and use of social media to discuss tobacco products. Recruitment occurred via Craig's List in states with varying levels of tobacco use including: KY (high), VA (mid), and California (low). Eligibility criteria included: 21+, English speaking and reported past 30-day snus or e-cigarette use. Interviews were recorded, transcribed and thematically coded.
Results: Four e-cigarette users, three snus users, and one e-cigarette/snus user were interviewed. Themes that emerged included perceptions of health and social impacts, as well as the experiential aspects of each product both on its own and in comparison to traditional cigarettes and other tobacco/nicotine products.
Conclusions: The interviewees represented a range of e-cigarette and snus use patterns, reported varied experiences with these products, and expressed perceptions that were informed by health beliefs and social norms. Respondents reported a low knowledge of evidence-based information about health impacts associated with both snus and e-cigarettes. These exploratory interviews provided an opportunity to learn more about the interviewee's own frameworks and the language used to describe use of e-cigarettes and snus. Reflecting overarching themes and considerations, findings were used to inform qualitative coding of content from Internet forums as part of the development of a post-market surveillance program.
Financial Support: Inflexxion, Inc., Altria Client Services Inc.

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A PROSPECTIVE STUDY OF YOUTH'S NONMEDICAL USE OF OPIOIDS, ANXIOLYTICS AND SEDATIVES.

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Aims: To determine whether adolescents' recent medical use of opioid analgesics, anxiolytics or sleeping medications is associated with an increased incidence of nonmedical use one year later. Compared to Group A, Group B respondents will demonstrate a higher incidence of nonmedical use opioids, anxiolytics and sedatives at Time 2, and will endorse both sensation-seeking and self-treating motivations.

Methods: A longitudinal study using annual web-based surveys was conducted in five secondary schools between 2009 and 2012. At Time 1 respondents self-selected into mutually exclusive groups: Group A was the no exposure group (n=1,287), never having used opioid analgesics, anxiolytics or sedatives. Group B (n=314) was exposed medically to opioids, anxiolytics or sedatives within the past 12 months, and had possessed their own legal prescriptions for the medications. The sample was comprised of 1,601 adolescents with an average age of 14.8 years (SD=1.9). Sixty-five percent (65.4%) were White/Caucasian, 28% were African-American, and the rest were from other ethnic groups (Asian, Hispanic, and American Indian/Alaskan Native). The sample was evenly distributed by sex and grade.

Results: At Time 1, most in Group B had been given a prescription for opioid analgesics (89.9% received opioids, 12.5% anxiolytics and 10.3% sedatives). At Time 2, Group B had a significantly increased incidence of nonmedical use of opioids, anxiolytics or sedatives when compared to Group A (AOR, 3.32 [95% CI 2.04-5.38] p<0.001), with increased odds of engaging in sensation seeking (AOR, 5.62 [1.94-16.23] p<0.001) as well as self-treatment motivations (AOR, 2.96 [1.77-4.93] p<0.001) with the nonmedical use.

Conclusions: A legal prescription for a controlled medication at Time 1 increases an adolescent's risk of nonmedical use one year later, both for sensation-seeking and self-treating motivations.

Financial Support: This research was supported by research grants R01DA024678, R01DA031160, T32DA007267 from the National Institute on Drug Abuse, National Institutes of Health.

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WITHDRAWN

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MALMö TREATMENT REFERRAL AND INTERVENTION STUDY: EFFECTIVE REFERRAL FROM SYRINGE EXCHANGE TO TREATMENT FOR HEROIN DEPENDENCE.

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Aims: Syringe exchange has been suggested as a potential conduit to treatment for drug addiction, but this never has been documented in Europe. The results from a few US trials have been varying between 16-70% successful referrals even with motivational and financial incentive.

The present study aims to assess effectiveness of an syringe exchange programme for referral of heroin addicts to evidence-based treatment, and to assess, in an RCT design, the contribution of a case management intervention.

Methods: Heroin addicts attending the syringe exchange of Malmö, Sweden, who are willing to participate, are referred to maintenance treatment and randomized to either a strength-based case management intervention in order to facilitate referral, or to referral-only. If eligible for treatment, patients are initiated on the maintenance treatment after 11 days. Study outcome is successful transfer from syringe exchange to treatment initiation.

Results: After applying exclusion criteria, 79 heroin users at the syringe exchange programme were addressed and offered to participate in the study. 75 patients turned up for baseline interview and randomization and of those 74 that is 99% of included subjects showed up for medical assessment. Out of the total of 74 that showed up for medical assessment 71 (96%) successfully started treatment. After 6 months 63 patients remained in treatment (89%).

Conclusions: Our data indicate that syringe exchange in a Swedish setting can be efficient for transferring heroin-dependent patients to evidence-based treatment. Strength-based case management intervention did not predict referral to treatment initiation. We also showed high retention rates at 6 months.

Financial Support: Skane region
Swedish research council for health, working life and welfare

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REAL-TIME FUNCTIONAL MRI FEEDBACK ATTENUATES CUE-INDUCED CRAVING IN NON-TREATMENT-SEEKING NICOTINE-DEPENDENT SMOKERS.

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Aims: The prefrontal cortex (PFC) plays an important role in cue-induced craving. Realtime functional Magnetic Resonance Imaging (rtfMRI) provides an individual with feedback about their neural activity during a task. We hypothesized that compared with no feedback, "real" feedback from a region of interest (ROI) in the PFC would significantly attenuate cue reactivity in nicotine-dependent smoker

Methods: In a single-blind controlled trial, nicotine-dependent smokers (N=49) were randomized to either a real (R) or no (N) feedback group. Participants completed three rtfMRI sessions, and two follow-up visits. An ROI was established through a "crave" run in which the participants were instructed to crave when viewing smoking cues. A thermometer bar depicting activity in the ROI (anterior cingulate or medial PFC) was 'fed-back' during three "reduce" craving scans while participants viewed smoking and neutral cues. Participants were asked to reduce craving and the activity in the ROI. In a human laboratory cue reactivity session conducted after each scanning visit, psychophysiologic and self-report response to nicotine cues were measured.

Results: There was a significant effect of group for heart rate (F=14.13, p<0.001) and skin conductance (F=9.67, p<0.01), with the R group exhibiting lower responses to the cues than the N group. There were significant group differences in urge to smoke (F=4.52, p<0.05) and craving (F=4.00, p=0.05), with the R group reporting a lower urge to smoke and lower peak craving than the N group. There was a significant group effect on the percent BOLD signal change in the ROI, with the R group exhibiting a lower BOLD response in the ROI than the N group.

Conclusions: These data suggest that rtfMRI feedback from a patient-tailored ROI can attenuate craving and regional brain activity in nicotine-dependent smokers. Future work is needed to translate these findings to clinical practice.

Financial Support: Supported by 5R33DA026085

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RISK FACTORS OF PSYCHOSIS AMONG AMPHETAMINE USERS: A PROSPECTIVE STUDY OF CLIENTS IN THE SWEDISH CRIMINAL JUSTICE SYSTEM.

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Aims: The aim of this prospective study was to investigate which risk factors mediate the risk of hospitalization due to psychosis in a cohort of amphetamine users in the Swedish criminal justice system.
Methods: Amphetamine-using prison inmates or clients of other correctional facilities in Sweden were identified using the Addiction Severity Index (ASI) interview. Between 2001 and 2006, a total of 1709 individuals were identified. A follow-up of the subjects, using national registry data, was conducted in 2010. The outcome measure was hospitalization for primary or substance-induced psychotic episodes during the follow-up period. Data was analyzed in a multivariate logistic regression model.
Results: Age of onset of amphetamine use, number of years used, and use in the month prior to baseline interview were all unrelated to risk of future hospitalization due to psychosis. Prior psychiatric hospitalization and experience of hallucinations not related to drug use, as well as being born outside of a Nordic country or being homeless, were all positively linked to hospitalization due to psychosis.
Conclusions: This study demonstrates that, in a cohort of amphetamine users within the criminal justice system, prior psychiatric morbidity and demographic risk factors are more important than baseline patterns of amphetamine use in predicting future risk of hospitalization due to psychosis. These findings suggest the need for a more integrated understanding of amphetamine use and psychosis.
Financial Support: Financed by internal funding from University of Oslo

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HEROIN AND PRESCRIPTION OPIOID USERS: CHARACTERIZATION IN A CANADIAN FEDERAL CONTEXT.

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Aims: While the literature suggests that prescription opioid (PO) abuse is a growing public health issue in the general population, it is unclear if this is also the case for those residing in federal correctional institutions. The objectives of this study were to characterize male inmates within federal correctional institutions throughout Canada who self-reported their drug of choice as heroin (H), PO and a combination of PO and H, to compare these three groups on demographics, substance use history, offence history and criminogenic risk
Methods: Male inmates (n=784) from five federal institutions who had completed the Computerized Assessment of Substance Abuse (CASA) between April 1, 2006 and March 31, 2010 were included in this study. The Offender Management System (OMS), an electronic administrative database, was used to retrieve additional information.
Results: Overall, 6.8% of offenders who completed the CASA in the period examined, reported opioids as their drug of choice in the 12 months prior to their arrest. Of these, 61.2% claimed to have used only PO, 21.3% reported using H only and 17.5% both (H+PO). The three groups did not differ significantly in terms of demographic variables or criminogenic risk. Seventy-two percent of the offenders had a substantial to severe drug use problem and 19% had a moderate drug use problem. The H+PO group was significantly more likely than the PO or H groups to have a substantial to severe drug use problem. The H+PO and H users were significantly more likely than PO only users to be under the influence of drugs on the day of their current offence, and to have committed their current offence to support their drug habit. Similarly, high proportions of offenders (81% overall) in each group reported that drugs made their judgement worse at the time of their offence.
Conclusions: The findings provide a better understanding of these three population groups and the impact of their drug use on criminal behaviour.
Financial Support: Health Canada and Correctional Services Canada

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EFFECTS OF MATERNAL OPIOID MAINTENANCE THERAPY ON NEONATAL OUTCOMES: METHADONE VS. BUPRENORPHINE.

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Aims: Opioid maintenance therapy (OMT) with methadone (METH) and buprenorphine (BUP) during pregnancy bears the risk of neonatal abstinence syndrome (NAS) since opioids as other medications cross the placenta. Previous studies reported favourable NAS and neonatal outcomes for BUP compared to METH. The aim of the present study was to assess effects of maternal OMT (METH vs. BUP) on NAS duration and severity as well as neonatal outcomes and to evaluate differences of therapy methods and neonatal outcomes over the past decade.
Methods: A prospective, standardized, observational study design was used for analysis of 68 mothers in multidisciplinary treatment and their neonates. 39 women were maintained with METH (mean dose at delivery: 58.62 mg/day) and 29 with BUP (9.60 mg/day). NAS was assessed by a modified Finnegan scale and treated with standardized pharmacological intervention.
Results: BUP showed a significant benefit in dose of medication needed for treatment of NAS (mean morphinhydrochlorid dose 22.8 mg vs. 8.65 mg, p=0.006) and length of NAS-treatment (METH: 18.9 days, BUP: 12.4 days; p=0.021). No significant differences between METH and BUP exposed neonates were observed for neonatal outcomes (birth weight, length, head circumference and gestational age; all p>.1). Comparison to data gathered in a comparable study design 10 years ago showed that for both groups duration of pregnancy could be prolonged from 38th to 39th week of gestation (p=0.033) and length of hospital stay was shortened from 27 to 18 days (p=0.024) for all children and from 33 to 22 days (p=0.024) for children in NAS treatment.
Conclusions: OMT with BUP compared to METH during pregnancy has several advantages in terms of NAS parameters. However, a broader concept of medical treatment is important for both medications and enables a multidisciplinary care approach. A standardized pharmacological approach in pregnant women and their neonates reduces treatment costs.
Financial Support: The project was supported by the Austrian National Bank.

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COCAINE DEPENDENCE AND CHILDHOOD MALTREATMENT ARE ASSOCIATED WITH ALTERED CONFIGURATIONS OF PERSONALITY TRAITS.

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Aims: Addictions are debilitating disorders that are highly associated with personality abnormalities. Early life stress (ELS) is an established risk factor for addiction and personality disturbances, but the behavioral and neural representations of the relationships between addiction, ELS and personality organization are poorly understood. We hypothesized that subjects with ELS history and cocaine dependence express deviations in personality trait expression and organization compared to control subjects.
Methods: Ninety-five human research participants (37 females, mean age 37.8 ± 8.8) were assessed for cocaine dependence (-/+) and ELS history (-/+) and were grouped factorially. NEO-FFI personality measures were compared between the groups to examine addiction- and ELS-related personality differences using a one-way ANOVA ($P < 0.05$) with a Bonferroni correction ($P < 0.0083$). The k-means clustering method was used to uncover personality configurations within the sample; these clusters were stratified across subject groups ($\chi 2$ test, $P < 0.05$).
Results: Trait expression differed significantly across subject groups. Cocaine-dependent subjects with a history of ELS (cocaine+/ELS+) displayed significantly greater neuroticism and lower openness, agreeableness, and conscientiousness than controls (cocaine-/ELS-). The cluster analysis resulted in four distinct personality profiles: Open, Gregarious, Dysphoric, and Closed. Distribution of these profiles across subject groups differed significantly. Most cocaine-dependent subjects were either Dysphoric or Closed; the cocaine-/ELS+ group was predominately Open, and the cocaine-/ELS- (control) group was predominately Gregarious.
Conclusions: Cocaine dependence and ELS were significantly and differentially associated with altered expression of individual personality traits and holistic personality profiles.
Financial Support: NIH NIDA 5R01DA019999 and 5T32DA022981; NIH CTSA program UL1TR000039 and KL2TR000063

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EVALUATION OF LISDEXAMFETAMINE ALONE AND LISDEXAMFETAMINE + MODAFINIL FOR COCAINE USE DISORDER.

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Aims: Modafinil and sustained release (SR) amphetamine (AMPH) have each shown efficacy for cocaine use disorder, albeit with equivocal results. We hypothesize that a combination medications approach may be more efficacious for cocaine use disorder. The specific aim of this study is to determine the effects of treatment with lisdexamfetamine alone, and lisdexamfetamine + modafinil, versus placebo, on the subjective and reinforcing effects produced by cocaine in non-treatment-seeking individuals with cocaine use disorder.
Methods: In this ongoing study, participants are being recruited from the Houston metropolitan area. All participants meet DSM-IV criteria for cocaine use disorder, and are not seeking treatment. Participants are randomized to placebo, lisdexamfetamine (30 mg/day), or modafinil (200 mg/day) + lisdexamfetamine (30 mg/day) for 4 days. On day 4, participants complete two self-administration sessions involving 5 choices for either cocaine (20 mg/infusion) or saline. Primary outcome measures include number of choices made for cocaine/saline, and changes in subjective effects and cardiovascular measures.
Results: To date, the majority of enrolled participants (N=18) are African American males who smoke cocaine. The majority of individuals also smoke cigarettes, and use alcohol and marijuana. In comparison to saline, exposure to cocaine resulted in significantly greater choices for an infusion, increased heart rate and blood pressure, and greater self-reports of positive subjective responses (e.g., "High", "Any Drug Effect") (all p's < 0.001). To date, no medication effects have been observed among treatment groups as compared to placebo.
Conclusions: The preliminary analyses did not reveal any significant effects produced by the test compounds; however, the group sizes are small (N~ 6/group) and data collection is ongoing (final N=20/group).
Financial Support: Supported by DA023625 (DLG). This work was conducted at, and supported by, the Michael E. DeBakey VA Medical Center, Houston, TX

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SCREENING AND BRIEF TREATMENT FOR ILLICIT DRUG USE IN PRIMARY CARE: FEASIBILITY AND ACCEPTABILITY.

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Aims: Brief intervention in primary care settings for illicit drug use has a mixed track record in reducing drug use. We are conducting a randomized clinical trial of a brief intervention (SBIRT) against a 2-6 session intervention of brief treatment in three urban federally qualified healthcare centers (FQHCs). Feasibility and acceptability results are reported here.
Methods: Primary care patients were screened for risky substance use (alcohol and drug) as they attend regularly scheduled appointments. Consenting patients who screened positive were randomized to receive: 1) SBIRT, conducted in one session and boosted with a 10-15 minute follow-up within the next month, or 2) SBIRT+, 2-6 sessions incorporating MET, CBT, and boosted with ongoing monthly brief recovery check-ups.
Results: 7,162 patients were prescreened, and 745 patients demonstrated drug or alcohol risk on the DAST or AUDIT; 414 patients have currently enrolled. Enrolled patients demonstrate a relatively even split between primary alcohol (35%), primary marijuana (37%) and other illicit drugs (28%). Patients reported frequent drinking days (M=10.07, SD=9.89) and days of drug use (M=14.63, SD=12.08) in the past 30 days. Engagement with both study conditions has been acceptable; SBIRT+ patients attended M=3.56 sessions (SD=1.74). Patient satisfaction and perception of utility regarding clinical procedures has been very high. Approximately 49% of patients to date have been referred to addiction treatment, and 24% have entered treatment.
Conclusions: Screening and onsite brief intervention / brief treatment is feasible in urban FQHCS. Heavy substance users enrolled in an ongoing trial in primary care find returning for multiple brief treatment sessions acceptable.
Financial Support: Commonwealth of Pennsylvania Department of Health SAP#4100055578

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EVALUATION OF AN ELECTRONIC INFORMATION SYSTEM TO ENHANCE PRACTICE AT A MEDICATION-ASSISTED OPIOID TREATMENT PROGRAM.

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Aims: START is an outpatient substance abuse program that provides primary care for approximately 3000 adults in NYC. We received funding to evaluate implementation of an electronic medical record integrating all services.
Methods: Quality, Satisfaction, Productivity, and Financial Performance were evaluated utilizing a pre and post-implementation research design. The capabilities of the electronic system were utilized to evaluate Quality, Compliance, and Productivity in all disciplines. This was particularly timely, given that the substance abuse regulatory agency in NY instituted Ambulatory Patient Groups as their payment methodology.
Results: The research found that for: (1) Quality, pre-implementation annual medical assessments and annual, 30-day and 90-day multidiscipline assessments were timely for 83% and 70%, 72%, and 42% of cases, respectively. Post-implementation, timeliness was 97% and 96%, 87%, and 70% respectively, all highly statistically significant improvements. Hepatitis C viral load was appropriately performed in 85% of cases pre-implementation and 81% post-implementation; a non-significant difference; (2) Satisfaction, there was no change for patients and a non-significant upward trend post-implementation for staff; (3) Productivity, there was a decline post-implementation; reaching statistical significance for counselors; and (4) Financial Performance, there was no significant change. The ability to generate monthly reports covering Quality (opiate and cocaine-free status for >80% of patients; HIV viral load suppression; HgbA1c <7 for diabetes mellitus; and BP <140/90 for hypertension); Compliance (timely completion of behavioral and medical assessments; meeting or exceeding state targets for vocational status); and Productivity (all disciplines) resulted in improved performance over time.
Conclusions: Our ability to exploit system capabilities to provide timely feedback allowed us to navigate changes in reimbursement and documentation, including changes resulting from the Affordable Care Act.
Financial Support: Supported by the National Institute on Drug Abuse (R01 DA022030)

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TOBACCO OUTLETS AND TOBACCO USE IN BALTIMORE CITY FROM 2004-2009.

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Aims: To compare the distributions of tobacco outlet density (TOD) and past month tobacco use in Baltimore City.
Methods: This exploratory data analysis sampled participants (n=327) from the Johns Hopkins Baltimore Prevention Project's (BPP) 2nd Generation Trial. In 1993, participants selected in the BPP trial were representative of the number of students entering 1st grade in 9 public elementary schools in Baltimore City. Participants were followed through adulthood. The current sample was predominately African American (96%), male (52%), on average 22 years old in 2009, and included participants who remained in Baltimore City from 2004-2009. Licensed cigarette retailers (i.e., tobacco outlets) in Baltimore City from 2004-2009 were obtained from the Baltimore City Circuit Court. Tobacco use prevalence, and TOD were assessed yearly.
Results: The distributions of past month tobacco use and TOD were parallel among youth who were 1 to 4 years post high school, but not among younger groups. TOD in Baltimore City decreased by 36% from 2004-2009. TOD was lowest in 2008 (n=860), as compared to 1830 tobacco outlets in 2004. TOD increased 35% from 2008-2009. Past month tobacco use ranged from 13%-17%, and was lowest in 2008 when the TOD was lowest. Past month tobacco use increased from 15%-17% in the 11th grade (2004) through one-year post high school (2006), despite a decrease in TOD during this time. Past month tobacco use decreased to 15% by 2009.
Conclusions: This study lends to the generation of new hypotheses about the relationship between TOD and tobacco use. For example, age may moderate the influence of TOD on tobacco use. Additionally, research should explore and potentially capitalize on the predictors of the decline in tobacco outlets in Baltimore City, as this may ultimately reduce tobacco use.
Financial Support: Supported by NIDA grant T32DA007292 (P.I. Debra Furr-Holden, PhD).

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PATIENTS' ECONOMIC CONSIDERATIONS OF TREATMENT FOR METHAMPHETAMINE AND OPIATE USE AT AN INNOVATIVE DRUG TREATMENT CENTER IN MALAYSIA.

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Aims: Cure and Care (C&C) centers are new, voluntary rehabilitation programs in Malaysia that provide comprehensive services including access to opioid substitution therapy to meet the individualized health needs of drug users. To understand patients' receptiveness to the new harm-reduction rehabilitation model from their perspective, a qualitative study was conducted to complement a mixed-methods study evaluating individuals' treatment outcomes and satisfaction with services provided.
Methods: A convenience sample of inpatients (N=20) at Cure and Care center in Kota Bharu, Malaysia participated in semi-structured, in-depth interviews conducted June-July 2012. Content analysis identified salient themes about drug and family history and barriers to treatment.
Results: Data analysis revealed themes relating to the low cost of drugs and the positive and negative aspects of patients' previous drug use, which centered around work productivity. Patients explained that pil kuda (methamphetamine) would make them appear hardworking and earn praise from employers until their dependence made them erratic. Patients primarily began using drugs with their friends and described patterns of avoidance and reacquaintance, which patients believed caused relapse.
Conclusions: Responses show that patients primarily use an economic framework to describe previous drug use, perceived benefit of drug use as well as explanations for decision making surrounding their self-described progression of drug behaviors and type of drugs used. Patients used their work productivity to assess the efficacy of the treatment they receive at the Cure & Care center. This information should be used for future empirical studies to validate and confirm the center's ability to reduce drug relapse rates among patients.
Financial Support: High Impact Research Grant from University of Malaya, Yale College Fellowship for Research in Health Studies, Gary Stein Memorial Fellowship, Linck Summer Fellowship.

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LONGITUDINAL TRAJECTORIES OF DISINHIBITORY PERSONALITY AND BEHAVIORAL CONSTRUCTS ACROSS EARLY TO MIDDLE ADOLESCENCE.

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Aims: Adolescent substance use and abuse show associations with increases in disinhibitory constructs, including sensation seeking (SS), risk taking propensity (RTP), and impulsivity. However, the trajectories of these constructs from early to middle adolescence remain largely unexplored. We aimed to provide an investigation of the course of these disinhibitory constructs from early to middle adolescence. In doing so, we examined race and gender in relation to construct changes over time.
Methods: The study consisted of 277 early adolescents recruited as part of a 5-year longitudinal study (44% girls; 49% White, 35% Black; Mage at first wave = 11.00). RTP, impulsivity, and SS were assessed using well-established assessments including the Balloon Analogue Risk Task-Youth version, Eysenck Impulsivity Subscale version, and the Brief Sensation Seeking Scale, respectively. Follow-up assessments were conducted annually for 5 consecutive years.
Results: Hierarchical Linear Modeling analyses showed that sensation seeking increased in a linear fashion ($\beta = 0.83$, SE = 0.37, $p = 0.03$), whereas RTP and impulsivity demonstrated curvilinear changes ($\beta = -0.80$, SE = 0.18, $p < 0.001$ and $\beta = -0.32$, SE = 0.08, $p < .001$, respectively). Specifically, RTP increased in the first four waves of assessment but did not show changes at the last assessment wave. Impulsivity, on the other hand peaked at wave four before subsequently declining. A comparison between females and males and Black and White adolescents suggested that these groups' trajectories were similar.
Conclusions: These findings replicate and extend earlier work indicating that these risk factors increase across early adolescence and begin to level-off during middle adolescence. Understanding the natural course of these disinhibitory core constructs is critical in directing future work on the prevention and intervention of adolescent substance use and abuse.
Financial Support: University of Maryland, College Park

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MISUSE OF ALPRAZOLAM AMONG PEOPLE WHO INJECT DRUGS: A PRESCRIPTION FOR HARM?

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Aims: Alprazolam prescriptions have dramatically increased in Australia, with use doubling in a decade (6 DDD/1,000 population/day in 2011). Due to increased morbidity in overdose and evidence of misuse, alprazolam will be placed in a higher regulatory schedule than other benzodiazepines from 2014. We aim to examine the extent of alprazolam use in an Australian national sample of people who inject drugs, and to determine whether alprazolam use is associated with harms beyond that associated with use of other benzodiazepines.
Methods: Cross-sectional face-to-face interviews with 1599 frequent (at least monthly) injecting drug consumers (IDU) in 2011-12.
Results: In the preceding six months, 36% reported no benzodiazepine use, 24% benzodiazepines other than alprazolam; and 41% reported illicit alprazolam use. One-fifth (23%) reported daily benzodiazepine use. Eight percent had recently injected benzodiazepines, typically this was alprazolam (7%). Multivariate regression models, controlling for demographics, demonstrated that, compared to those who had used non-alprazolam benzodiazepines, IDU that did not take benzodiazepines had higher levels of physical and mental functioning (SF-12). Compared to IDU using other benzodiazepines, alprazolam users were more likely engaged with opiate substitution treatment (AOR 1.54), to have poorer mental health (SF-12), and to have committed crime in the past month (AOR 1.62) or been arrested (AOR 1.75). Hierarchical regression modelling demonstrated that the association between extent of alprazolam use and crime remained even after controlling for the extent of use of all other types of benzodiazepines.
Conclusions: Alprazolam is associated with incrementally greater harm than other benzodiazepines. Given this, its attractiveness to IDU, and the absence of additional therapeutic benefit over other drugs in this class, particular caution to its use in this population is warranted.
Financial Support: Australian Government Department of Health and Ageing.

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REPRODUCTIVE HEALTH NEEDS AMONG DRUG TREATMENT CLIENTS.

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Aims: Previous studies have indicated gaps in reproductive health care for drug and alcohol treatment clients.The goal of this study was to determine the reproductive health needs of drug treatment clients in Baltimore City, Maryland.
Methods: A survey instrument was adapted from the National Survey of Family Growth and administered to male and female treatment clients in residential, outpatient, and methadone maintenance sites. The survey captured sexual activity, pregnancy intention, contraceptive use, sexually transmitted infections (STI), health care utilization and access, as well as basic demographic factors. Surveys were collected for one year starting in August 2012. Data were analyzed using STATA v 11.
Results: The survey was completed by 95 men and 115 women from 4 distinct clinical sites. Age was similar by gender (mean=42 for men and 39 for women). 83% of the women were under 50 and had on average 3.5 prior pregnancies and 2.4 prior births. Fair/poor health was reported by 24% of men and 31% of women. The majority of clients were sexually active (73% women, 85% men) and did not want to be pregnant (77%) or did not want their partner to be pregnant (63%). However contraceptive use was rare with 42% of men and women reporting no method in past 12 months. Condoms were the most commonly used method reported by 48% of men and 42% of women. Other methods were extremely rare. Although almost all clients had accessed health care in the prior year and about 70% had received STI screening, only 6% of men and 13% of women reported receipt of any contraception counseling. Women desired family planning services more than men, with 66% of women versus 31% of men saying they would use family planning services at their treatment site if available.
Conclusions: There are clearly unmet reproductive health needs among treatment clients in Baltimore City. Compared with STI screening, contraceptive access and counseling is lacking.
Financial Support: None

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A PROGRESSIVE RATIO DETERMINATION OF THE RELATIVE REINFORCING EFFECT OF METHYLPHENIDATE VERSUS COCAINE BY INTRAVENOUS SELF-ADMINISTRATION TESTING IN RATS.

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Aims: Methylphenidate (MPD) is a psychostimulant that is widely used to treat ADHD. Microdialysis has revealed that MPD evokes rapid, large increases in dopamine and noradrenaline efflux in the brain with no dose-effect ceiling, which is analogous to the effects of the amphetamine releasing agents (Heal et al, 2012, Curr Top Behav Neurosci, 9: 361 390). We have determined the relative reinforcing effect of MPD by comparing its break-point versus 2 reinforcing doses of cocaine.

Methods: Eleven male Sprague-Dawley rats were trained to self administer cocaine (0.32mg/kg/injection, iv) on a fixed ratio (FR2) schedule of reinforcement. After undergoing saline extinction, rats were switched to MPD (0.1 mg/kg/injection) or cocaine (0.32 or 0.1 mg/kg/injection, iv). When stable positive reinforcement had been established, the break-point for operant responding was determined using an ascending progressive ratio (PR) schedule of reinforcement in a 2.0hr test session.

Results: Compared with saline, MPD and both doses of cocaine served as positive reinforcers (mean total infusions/session ± SEM: MPD = 18.4 ± 0.7 [n = 6], $p<0.001$; Cocaine [0.1 mg/kg/injection] = 18.2 ± 0.8 [n = 6], $p<0.001$; 0.32 mg/kg/injection = 16.2 ± 0.6 [n = 7], $p<0.001$). On the PR schedule, the break-point of operant responding (mean lever-presses ± SEM) for the higher dose of cocaine (43.0 ± 2.8 [n = 7]) was significantly higher ($p<0.01$) than for the lower dose (14.1 ± 1.7 [n = 6]). The break-point for MPD (37.8 ± 7.8 [n = 6]) was not significantly different from that of the higher dose of cocaine, but it was significantly higher ($p<0.01$) than the lower dose.

Conclusions: The findings confirm that MPD serves as a positive reinforcer in rats trained to self-administer cocaine. The break-point analysis revealed that the relative reinforcing effect of methylphenidate is equal to that of a highly reinforcing dose of cocaine. These results provide additional evidence to demonstrate that MPD and cocaine possess similar pharmacological and reinforcing characteristics.

Financial Support: None

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REDUCTION OF ADULT HIPPOCAMPAL NEUROGENESIS VIA CRANIAL IRRADIATION ENHANCES MORPHINE SELF-ADMINISTRATION AND MORPHINE-INDUCED LOCOMOTOR SENSITIZATION.

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Aims: Drugs of abuse dynamically regulate adult hippocampal neurogenesis (AHNG), a process important for hippocampal-dependent functions such as context learning and memory, context discrimination, and regulation of the stress response. To test the hypothesis that AHNG is involved in the vulnerability to morphine addiction, we assessed whether ablation of AHNG enhances vulnerability to addiction during morphine self-administration (MSA) and morphine locomotor sensitization (MLS).

Methods: Male Sprague-Dawley rats (~6 weeks old) were exposed to either sham treatment (Sham) or image-guided cranial x-ray irradiation (IRR) to eliminate new hippocampal neurons. Ablation was confirmed via absence of doublecortin+ immature neurons. Six weeks post-IRR when inflammation subsided, rats began either MSA (Sham=16, IRR= 15) or MLS (Sham=12, IRR=12).

Results: For MSA, IRR rats self-administered more morphine vs. Sham rats ($p<0.019$). This was not a general enhancement of learning, motivation, or locomotion, as operant learning and locomotor activity were unchanged. After 28 days of withdrawal, IRR rats exhibited higher context-induced reinstatement than Sham rats ($p<0.038$). In the separate group of rats used for MLS, IRR rats exhibited a dose-dependent enhancement of morphine locomotor sensitization, with a greater increase in beam breaks vs. Sham rats at 5 mg/kg ($p<0.003$), but similar increases at 10 mg/kg, suggesting a ceiling effect.

Conclusions: Along with previous studies, these data indicate that reduced AHNG confers vulnerability for multiple classes of drugs. This suggests that therapeutics to specifically increase or stabilize AHNG could aid in preventing initial addiction as well as future relapse. Mechanistic studies are ongoing to explore the involvement of AHNG in the neural circuitry underlying the morphine-induced activation of the hippocampus and downstream brain areas, and how this circuitry is altered when adult neurogenesis is ablated.

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OPIOID SUBSTITUTION THERAPY IN NEW SOUTH WALES 2001-2012: COMPARISON BETWEEN BUPRENORPHINE AND METHADONE.

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Aims: The aims of this study were to: compare the characteristics of first-time entrants into methadone and buprenorphine treatment; track treatment discontinuation and re-entry with methadone and buprenorphine; and, examine the factors associated with an individual's risk of leaving their first OST treatment episode.

Methods: This is a retrospective data linkage study. All episodes of opioid substitution treatment recorded in New South Wales Australia (1985-2010) were linked to custody episodes (2000-2012) and mortality information. Analysis was undertaken on 32,033 individuals receiving OST between 1st August 2001 and 31st December 2010.

Results: A total of 15,600 individuals commenced their first OST treatment episode between 1st August 2001 and 31st December 2010. Of these, 46% (n=7,183) commenced buprenorphine and 54% (n=8,417) methadone. Approximately half of all individuals (56%) who commenced buprenorphine spent less than 3 months ion treatment, compared to 30% who had commenced methadone. Furthermore, those on methadone had the highest rate of retention in treatment at 12 months (44%) compared to buprenorphine (25%). Receiving buprenorphine in the community was associated with the greatest risk of leaving a first treatment episode (adjusted hazards ratio 1.57, 95% confidence interval 1.51-1.64).

Conclusions: Consistent with the results of the RCTs of treatment, individuals commencing methadone are retained longer in treatment than those commencing buprenorphine, independent of the setting in which treatment is received.

Financial Support: Support for this project was provided by the National Health and Medical Research Council.

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HOW DOES ONE MEASURE BUPRENORPHINE DIFFUSION? THE CHALLENGES OF ALTERNATIVE MEASURES OF SUCCESS.

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Aims: Researchers' examinations of the diffusion of buprenorphine have used several different metrics to measure diffusion, creating a challenge for interpreting findings and informing policy. We investigate different measures of diffusion at the state level and suggest an alternative definition of diffusion that draws upon multiple metrics. We demonstrate how this new metric of diffusion can be used to study facility factors associated with buprenorphine diffusion.

Methods: We use data from the 2004-2011 National Survey of Substance Abuse Treatment Services to examine how multiple measures of diffusion vary across states. We create an alternative categorical measure of buprenorphine diffusion that accounts for the number of patients per capita in 2006 (identifying them as early or late adopters depending on whether they exceed the mean number of patients per capita) and growth in either the percent of facilities treating patients with buprenorphine or the percent of patients receiving buprenorphine from 2004 to 2011. We then use this measure in a cross-tab analysis to identify facility characteristics that are associated with faster buprenorphine diffusion.

Results: Depending on which metric of diffusion is used, different patterns of diffusion emerge among the states, with some states performing relatively better on one metric, yet relatively worse on another. We create a multi-dimensional metric that incorporates both the number of patients per capita receiving buprenorphine at a given time and growth in the percentage of facilities treating patients with buprenorphine or patients receiving buprenorphine. Using this metric, we find that more rapid diffusion is associated with private, non-profit ownership (66% of facilities in early adopting/fast growth states, compared to approximately 55% in other states); focus on substance abuse treatment (66% of facilities in early adopting/fast growth states, compared to 49-60% in other states); OTP-certification (15% of facilities in early adopting/fast growth states, compared to 7-9% in other states); and larger facility size (32% of facilities in early adopting/fast growth states, compared to 19-26% in other states).

Conclusions: We find that a new measure of diffusion reveals important differences in the patterns of diffusion that would otherwise have been missed. The use of multi-dimensional metrics allows for a more in-depth understanding of diffusion of buprenorphine.

Financial Support: This work was supported by NIDA 1R01DA032881-01A1.

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COMPARING ABUSE OF EXTENDED-RELEASE VS. IMMEDIATE-RELEASE OPIOID ANALGESICS ADJUSTED FOR NUMBER OF PRESCRIPTIONS AND MORPHINE-EQUIVALENT DOSE.

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Aims: It has been suggested that abuse risk of extended-release (ER) opioids is greater than immediate-release (IR) opioids, but risk rates vary depending on the denominator. For example, widely prescribed IR opioids have high abuse rates, but dividing by their large Rx volume yields low per-Rx rates. Such estimates do not account for longer duration of ER Rxs and higher daily dose than IR Rxs, and may be a biased measure of relative risk. We compared abuse rates adjusted for various denominators.
Methods: The ASI-MV®, a computerized, clinical interview for adults in substance abuse treatment, collected self-report of past 30-day abuse of IR and ER opioids in 2011 to 2012. Abuse risk was adjusted for all ASI-MV assessments, and for number of Rxs, days per Rx, daily dose prescribed, and morphine-equivalent conversion.
Results: In the sample of 144,736 ASI-MV assessments, abuse per 100 assessments ranged from highest to lowest: IR hydrocodone (9.3), IR oxycodone combo (7.0), ER oxycodone (5.1), IR oxycodone single-entity (3.4); IR hydromorphone (1.7), ER morphine (1.4), ER oxymorphone (1.3) and ER hydromorphone (0.02). Abuse per 10,000 prescriptions dispensed yielded: ER oxymorphone (70.7), ER oxycodone (52.2), IR hydromorphone (35.6), ER morphine (12.7), IR oxycodone combo (12.0), IR oxycodone SE (11.8), ER hydromorphone (7.8), and hydrocodone (4.1). By per-1-million morphine equivalent mg dose, the order was IR hydromorphone (2.1), IR oxycodone combo (1.6), ER oxymorphone (1.3), ER oxycodone (1.2), hydrocodone (0.9), ER morphine (0.4), IR oxycodone SE (0.4), and ER hydromorphone (0.3).
Conclusions: Abuse of certain IR opioids is higher than ER opioids using population-adjusted rates and dispensed-dose adjustment. The order is reversed by prescription adjustment. The assumptions behind using prescription adjustment to measure abuse risk in the community need to be considered.
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HEALTH AND SOCIAL FACTORS ASSOCIATED WITH ALTERNATE ROUTES OF ADMINISTRATION OF PRESCRIPTION OPIOIDS AMONG YOUNG ADULT MULTIDRUG USERS.

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Aims: To examine health and social factors associated with alternate routes of administration (ARA) among young adult multidrug users in Miami.
Methods: Data are drawn from participants reporting recent (past 90 days) Rx opioid misuse (N=335) during baseline assessments in an ongoing behavioral intervention trial. Eligible participants were 18-39 and reported recent and regular use of club drugs (cocaine, ecstasy, LSD, GHB, ketamine, or methamphetamine) and misuse of Rx drugs.
Results: Participants identified as White (N=43), Black (N=56), Hispanic (N=225), and other (N=11). Mean age is 25 and 44% are female. Over 37% (N=126) reported ARA (injection, snorting, crushing, rectal/vaginal, smoking, parachuting). Compared to those who did not, participants reporting ARA were more likely to be White (p=.001), and to report severe mental distress (p<.000) and prior substance abuse treatment (p=.003). ARA was associated with participation in unprotected group sex (p=.031) as well as with social factors including lower satisfaction with family and living situations (p<.017) and more racially/ethnically diverse friendships (p=.001).
Conclusions: ARA is associated with many health and social factors including mental distress, dissatisfaction with family and living situation, and having diverse social and sexual networks. Social diversity may extend drug use practices to new groups, and sexual diversity, especially group sex, can facilitate HIV transmission across populations. Drug users who share injection equipment are at risk for infection/transmission of both HIV and HCV. Public health implications and needs for targeted intervention will be discussed.
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RECOVERYTRACK-EXTENDEDCARE™, A NOVEL MONITORING AND OUTREACH INTERVENTION.

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Aims: TRI has developed and implemented in community substance abuse treatment (SAT) programs RecoveryTrack™ (RT), a clinical, web-based, during treatment, Outcome Monitoring System. When clients are attending treatment, counselors conduct a brief multidimensional assessment during individual, in-person sessions on a systematic basis to monitor client progress and identify problems. RT was found to support treatment response and retention. As many clients drop out of SAT, more effective use of RT may also require monitoring and outreach when clients are not or only irregularly attending SAT. Thus, we developed RT-ExtendedCare (RT-E) and are testing its feasibility and efficacy.
Methods: Counselors in OP clinics were randomly assigned to provide RT-E or TAU; 39 new clients were assigned to receive RT-E (n=20) or TAU (n=19). RT-E counselors use monthly monitoring to guide the client's recovery (e.g., determine need for 'wrap-around' services, problem-solve with clients, encourage pro-recovery activities). When clients are not attending treatment, RT-E counselors attempt to contact them over the phone and conduct the RT-E assessment and, as warranted, help reengage the client in treatment (e.g., invite them back, resolve barriers) or support recovery in other ways. TAU counselors provide standard treatment and outreach.
Results: Of the 20 RT-E clients, 18 (90%) completed >1 (range 1-8) monitoring assessment. Counselors made >1 (1-10) outreach attempt to 16 clients (80%) and completed >1 (1-6) telephone RT-E assessment with 9 clients (45%). As part of TAU, 5 clients (26%) had >1 (1-8) outreach attempt. After 3 months, the majority of RT-E clients (n=13, 65%) are still attending treatment/RT-E phone sessions, while the minority of TAU clients (n=7, 37%) are attending treatment.
Conclusions: Preliminary indication is that RT-E is acceptable to counselors and clients, and positively impacts retention.
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FDA ABUSE-DETERRENT GUIDANCE. ASSESSING NEW TECHNOLOGIES.

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Aims: To provide an overview of the Food and Drug Administration (FDA) current experience on the evaluation of the properties of novel abuse deterrent (AD) formulations
Methods: The development of AD formulations that are less prone to abuse or misuse is a public health priority. To that end, the Center for Drug Evaluation and Research at FDA has developed guidance regarding the evaluation of AD opioid formulations (FDA/CDER, 2013)
Results: A phased three tier approach for premarketing assessment has been proposed for formulations with potential AD features. The first tier consists of in-vitro manipulation and extraction studies, aimed to evaluate the ease with which AD features of a new formulation can be defeated or partially compromised under experimental conditions. Pharmacokinetic/pharmacodynamic studies constitute the second tier. These studies are designed to understand the in vivo properties of the new formulation by comparing the pharmacokinetic profiles of the "manipulated" formulation with the intact formulation and other comparator drugs through one or more routes of administration, and to collect pharmacodynamic outcomes such as adverse events associated with the administration of the manipulated formulation. The third tier consists of evaluating the relative abuse potential of the AD formulation to that of a positive control and placebo in human abuse potential studies. The science of abuse deterrence is relatively new, and both the formulation technologies and methodologies for evaluating those technologies are rapidly evolving. As FDA gains experience in evaluating novel AD formulation technologies, new questions regarding the best science-based approaches to appropriately characterize these formulations arise.
Conclusions: As abuse-deterrent technologies and the methodology for evaluating those technologies are rapidly changing the FDA recognizes the need for additional scientific work to identify the best approaches to characterize these formulations
Financial Support: N/A

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WITHDRAWN

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INCREASING INCIDENCE OF HOSPITAL ADMISSIONS FOR OPIOID POISONINGS IN ADOLESCENTS AND YOUNG ADULTS: 2000-2009.

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Aims: Opioid misuse is a growing epidemic in adolescents and young adults in the US resulting in serious behavioral, medical and social consequences. This study aims to: (1) describe trends in the incidence of hospital admissions for opioid poisonings (OP) in a nationally representative sample of 12-20 year-olds (yo) and (2) compare trends in the incidence of OP to that of benzodiazepine (BZD; a prescription drug) and acetaminophen poisonings (APAP; a non-prescription drug).
Methods: We identified eligible hospital admissions among 12-20 yo from the 2000, 2003, 2006 and 2009 Kid's Inpatient Database (KID) using ICD-9-CM codes 965.00 (opium alkaloids unspecified), 965.01 (heroin), 965.02 (methadone), 965.09 (other opiates and related narcotics), 969.4 (BZD), and 959.4 (APAP). We calculated the incidence of admissions for OP, BZD and APAP by determining the weighted number of hospitalizations and using US Census data to establish the denominators and assessed trends with chi-square for linear trend.
Results: We identified 10,642 admissions for OP from 2000-2009; 61.3% (n=6,519) occurred in 18-20 yo, 31.6% (n=3,358) in 15-17 yo, and 7.2% (n=765) in 12-14 yo. Comparing 2000 to 2009, the incidence of OP admissions/100,000 person-years increased 314% for 18-20 yo (from 4.49-18.57; p<0.001), 129% for 15-17 yo (from 3.91-8.96; p<0.001); and 87% for 12-14 yo (from 0.95-1.78; p<0.001). Overall, the incidence of OP increased 221% (from 3.12-10.0; p<0.001). Comparatively, BZD poisoning increased 65% (from 7.76-12.82; p<0.001) and APAP poisonings decreased 16% (from 31.47 to 26.32; p<0.001). The majority (59.1%; n=6,289) of OP admissions had a co-occurring poisoning diagnosis; 23.6% (n=2,512) co-occurred with BZD, 14.2% (n=1,513) with APAP.
Conclusions: From 2000-2009, hospital admissions for OP increased for all age groups, with more than a three-fold increase in 18-20 yo. Admissions for BZD poisonings also increased, although not as substantially, and those for APAP poisonings decreased. The majority of adolescents and young adults admitted for OP had a co-occurring poisoning diagnosis.
Financial Support: NIDA 1K12DA033012-01A1.

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GENDER DIFFERENCES IN ACCEPTABILITY AND TREATMENT OUTCOMES OF INTERNET-BASED TREATMENT FOR SUBSTANCE USE DISORDERS.

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Aims: Digital technologies show promise for increasing treatment accessibility and improving quality of care, but little is known about potential gender differences. This secondary analysis uses data from a multi-site effectiveness trial, conducted within NIDA's Clinical Trials Network, of a computer-assisted behavioral intervention to explore gender differences in acceptability and treatment outcomes.
Methods: Men (n=314) and women (n=192) were randomly assigned to 12-weeks of treatment-as-usual (TAU) or modified TAU + the Therapeutic Education System (TES), whereby TES substituted for 2 hours of TAU per week. TES consists of 62 web-delivered, multimedia modules, covering skills for achieving and maintaining abstinence, plus prize-based incentives contingent on abstinence and treatment adherence. Outcomes were (1) abstinence from drugs and heavy drinking (last 4 weeks of treatment); (2) largest consecutive weeks of abstinence; and (3) retention. Acceptability was the mean score across five indicators (i.e., interesting, useful, novel, easy to understand, satisfaction).
Results: Findings showed that gender did not moderate the treatment effect on any of the three outcomes. Acceptability of TES did not differ by gender, however, a gender by acceptability interaction for abstinence (t=2.90, p=.004) and consecutive weeks of abstinence (t=2.23, p=.027) demonstrated that acceptability was significantly associated with abstinence, but only among women.
Conclusions: Gender may be an important factor to consider when thinking about using computer-assisted interventions, such as TES. Given the potential for technology to expand access and improve addiction outcomes, future research should strive to understand how to improve acceptability among women and ways to better integrate these interventions into traditional treatment.
Financial Support: This work was supported by grants from the National Institute on Drug Abuse: U10 DA13035, PIs Nunes, Rotrosen (National Drug Abuse Treatment Clinical Trials Network) and K24 DA022412, PI Nunes.

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TOBACCO USE AND EXPOSURE TO SECOND-HAND SMOKE IN MEXICAN PREGNANT WOMEN.

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Aims: The prevalence of smoking among women in Mexico is 12.6 % of the adult population.To assess the prevalence of tobacco smoking and of exposure to second hand smoke among pregnant women in a major pre-natal care clinic in Guadalajara (Mex).
Methods: To investigate smoking status and exposure to SHS during pregnancy, face-to-face interviews were conducted with 1481 women attending the pre-natal care clinic at the Hospital Civil of Guadalajara. Random urine samples were collected for cotinine tests. Participating women gave informed consent.
Results: The patients' mean age was 24.4 (± 7.3) years; their mean months of pregnancy was 6.7 (± 2.61). There were 1.5 % active smokers, while 29.1 % had smoked before pregnancy. Cotinine tests were positive in 3.2 % of a sample. Regarding SHS, 47.04 % lived with a mean 1.4 (± 0.9) smokers who smoked a mean 6.5 cigarettes. That included a husband/partner (35.7%), father (18.9%), mother (13.1 %), parents in-law (8.5 %), brothers (9.8%), sisters (3.6 %), brothers in-law (3.8 %), uncles/aunts (3.1 %), other (3.6 %). Outside their homes (including work), 26.5 % of the women were exposed to a mean of 3.4 (± 3.6) persons who smoked.
Conclusions: The prevalence of women smoking currently during pregnancy was relatively low in this sample. Most of the women reporting lifetime histories of smoking had stopped smoking by the time they were pregnant. The prevalence, however, of exposure to SHS in the sample (49.5%) was higher than in the Mexican general population. The findings from this sample need to be replicated at other sites. This study, the first of its kind in Mexico, underscores the need to find and implement ways to help pregnant patients limit their exposure to SHS.
Financial Support: This Project was funded by the Programa de Mejoramiento del Profesorado (PROMEP) of the Mexican Education department (SEP).

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ALCOHOL CONSUMPTION AND LONELINESS IN MID- AND LATE-LIFE.

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Aims: Loneliness, which has been associated with a range of negative health outcomes in later life, has been implicated as a risk factor for alcohol abuse. However, the relationship between loneliness and alcohol use is less clear. We sought to examine the association between loneliness and alcohol use in a sample of middle aged and older adults.
Methods: We studied participants aged 50 and older (n=957) from the 2002 wave of the Health and Retirement Study who reported the number of days per week they had consumed alcohol. Number of drinking days per week was categorized into tertiles (0, 1-3, and 4-7 days/week). Participants also responded to a 3-item questionnaire adapted from the Revised UCLA Loneliness Scale and were classified as "lonely" or "not lonely". Multinomial logistic regression analyses assessed the association between weekly alcohol consumption and loneliness.
Results: Overall, 7.7% of participants reported being lonely. After adjusting for demographic variables, medical conditions, smoking, and elevated depressive symptoms, loneliness was associated with a reduction in odds of more frequent alcohol consumption for both 1-3 days/week (aOR=0.44, 95% CI=0.20-0.99, p-value=0.046) and 4-7 days/week (aOR=0.41, 95% CI=0.17-0.98, p-value=0.044), compared to the 0 drinking days/week group.
Conclusions: Our results suggest that alcohol use may be a factor that reduces loneliness in a sample of adults aged 50 and older. This could suggest that socialization opportunities involve alcohol use; however, alcohol use could reduce feelings of loneliness regardless of social interaction. Caution in our findings is warranted given the host of negative physical and cognitive outcomes linked to overuse of alcohol in later life. Future research should explore how middle aged and older adults relate to alcohol both in social settings and while alone.
Financial Support: Dr. Canham and Ms. Mauro receive funding from the National Institute on Drug Abuse (T32-DA007292) and Mr. Kaufmann receives funding from the National Institute on Aging (F31-AG044052).

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SELF-REGULATION OF CRAVING-RELATED BRAIN ACTIVATION IN COCAINE USERS VIA REALTIME FMRI.

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Aims: Cue-induced drug craving is a key component driving relapse in cocaine dependence. The anterior cingulate cortex (ACC) is a critical region in the brain circuitry underlying cocaine craving and drug-seeking. Thus, modulation of the ACC has the potential to affect drug use outcomes. Building on studies using realtime (RT) fMRI to modulate nicotine craving, the aim of the current study is to examine the use of RT neurofeedback from the ACC to facilitate regulation of craving-related brain activation and subjective craving among cocaine-dependent individuals.
Methods: Following informed consent and screening/assessment procedures, current cocaine users completed a RT-fMRI experiment (n=5; ongoing), during which they viewed blocks of cocaine and neutral cues. In the first run, participants were asked to 'crave' and a craving-related region of interest was isolated in the ACC. During three subsequent neurofeedback runs, participants were instructed to decrease their craving and craving-related brain activation during exposure to the cocaine cues using the neurofeedback provided from the ACC. Self-reported craving was assessed following each run. Timeseries were extracted from the individually derived regions of interest. Percent signal change (PSC) was calculated for BOLD response during exposure to cocaine cues relative to neutral cues. PSC and craving was compared between 'craving' and 'neurofeedback' runs.
Results: Preliminary analysis demonstrated that craving-related activation in the ACC was decreased during the feedback runs, compared to activation during the craving run (paired samples t-test; p=.05). In addition, self-reported craving was reduced by 43% from pre- to post- neurofeedback.
Conclusions: These preliminary results suggest that cocaine users are able to decrease craving-related brain activation when provided with neurofeedback and instructions to reduce craving. This research suggests realtime neural feedback may be a potential adjuvant therapy, helping treatment-seeking individuals learn to control their craving and promote abstinence.
Financial Support: F32DA036329

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DISCRETE-TRIAL CHOICE PROCEDURE: METHAMPHETAMINE VS. AN ALTERNATIVE NONDRUG REWARD.

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Aims: Studies by Ahmed, Lenoir and colleagues demonstrate that the majority of male rats (over 90%) given a choice between cocaine and palatable food prefer the non-drug reward. We used a discrete choice procedure to assess whether this food preference generalizes to rats with a history of methamphetamine self-administration.
Methods: We initially trained non-food-deprived rats to lever press on a methamphetamine- or palatable food (45 mg TestDiet pellets)-associated lever during alternating daily 3-h sessions (FR1 reinforcement schedule; 0.1 mg/kg/infusion or 5 pellets per reward delivery). We then assessed progressive ratio responding for methamphetamine or food, and subsequently gave the rats discrete choice sessions under different conditions: following limited (3 h/d) or extended (6 h/day) access methamphetamine self-administration, training with a high unit dose of methamphetamine (0.2 mg/kg/infusion), priming injections of methamphetamine (0.5 and 1.0 mg/kg) or pellet exposure in the home cage (a satiety manipulation) prior to choice testing, and 21 abstinence days.
Results: We found that while rats demonstrated similar progressive ratio responding for methamphetamine and food, all rats strongly preferred the food reward, even when the food pellets were freely available in their home cage.
Conclusions: Results confirm and extend Ahmed and Lenoir's findings that the majority of laboratory male rats strongly prefer a palatable food reward over a psychostimulant drug. We currently use the discrete choice procedure to assess cue-induced drug seeking after short and extended periods of voluntary abstinence.
Financial Support: Supported by NIDA-IRP

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PREDICTORS OF SENTENCED INMATES' DRUG USE TRANSITION FROM COMMUNITY TO PRISON.

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Aims: Drug use in prison is a worldwide phenomenon, yet little is known about factors that predict transitions in drug use as individuals move from community to prison. Following the analysis presented at the 2013 CPDD Conference, were we reported transitions in drug use patterns prior and during imprisonment, in this second phase of analysis we present the covariates that significantly predict those transitions in a representative sample of the sentenced inmate population in the Puerto Rico prison system.
Methods: 1,179 inmates (89.7% response rate) participated in a structured questionnaire administered through 2 interview modalities: Computer Assisted Personal Interview for social and health variables and Audio Computer Assisted Self Interview for sensitive information. A stepwise latent transition analysis was conducted in MPlus. Since at an exploratory stage and due to power considerations, covariates influencing transition patterns were studied at the univariate level without adjustment for the other covariates. Included covariates were ADHD symptomatology, drug and alcohol dependence and recidivism.
Results: Covariates significantly predicting drug use transition were ADHD symptomatology and drug and alcohol dependence. 61% of inmates with ADHD symptomatology stayed in the high polydrug use class while 19% of those in the predominantly cannabis and non-prescribed medications transitioned to this same class. 57% of inmates with drug dependence remained in the high polydrug use class while most of those without the diagnosis transitioned (59%) from the predominantly cannabis and non-prescribed medications class to the low polydrug use class. This transition pattern is also observed in those with alcohol dependence.
Conclusions: Findings should inform services planning. Inmates should be screened for ADHD as well as for drug and alcohol dependence to establish an evidence-based intervention that reduces drug use given that prison is a high risk scenario for contagion with blood-borne viruses due to the frequency of injection under unsanitary conditions.
Financial Support: NIDA Grant # 2R24DA024868-03

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SURVEY STUDY OF CHALLENGING EXPERIENCES AFTER INGESTING PSILOCYBIN MUSHROOMS: DEMOGRAPHICS AND PHENOMENOLOGY.

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Aims: Although classic hallucinogens have relatively low physiological toxicity and do not produce compulsive drug seeking, they can produce adverse psychological reactions (i.e., 'bad trips'). An online survey study sought to better characterize such experiences.
Methods: Participants completed an anonymous online survey in reference to their most challenging experience after ingesting psilocybin mushrooms. The experience was required not to have occurred in the context of a research study. The questionnaire assessed the phenomenology of the experience.
Results: There were 1853 participants (mean age 29 yrs; 81% male; 50% college or graduate degree). 39% rated the experience as among the 5 most challenging experiences of their lives, and 34% rated the experience as among the 5 most meaningful of their lives. Scores on the Challenging Experience Questionnaire showed a reasonably high correlation with ratings of difficulty of experience (r=0.516), but not with ratings of the degree of spiritual significance (r=0.125). In contrast, scores on the Mystical Experience Questionnaire correlated moderately highly with spiritual significance ratings (r=0.658) but not with degree of difficulty (r=0.198). Consistent with known effects of psilocybin, participants endorsed visual effects (61%) and auditory (23%) and visual (21%) synesthesia. Anomalous experiences were endorsed, including: interactions with entities/persons not physically present (29%), convincing experiences of prior lives (10%), and experiences of jemais vu (17%). 11% reported that they put themselves or others at risk for physical harm during the experience.
Conclusions: Participants completed a survey about their most challenging experience after psilocybin. Scores of challenging experience and mystical experience showed different patterns of correlations. Visual and auditory effects and unusual phenomenology were reported.
Financial Support: NIH T32DA007209 and R01DA003889, and Heffter Research Institute

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WITHDRAWN

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RISK AND PROTECTIVE CORRELATES OF METH-ASSOCIATED EXTERNALIZING PROBLEMS AMONG EUROPEAN -AMERICAN AND U.S. LATINO/A METH-DEPENDENT USERS.

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Aims: Given the recent demographic shifts in the U.S., especially with regard to Latino/a immigrants in rural regions, research on METH use among Latino/a immigrants is needed. Further, little is known about protective factors in ethnic minorities. We examine risk and protective factors in METH-associated externalizing outcomes among White, European American and U.S. Latino/a METH-dependent users. We expected risk factors to be positively related to METH-associated externalizing problems and protective factors to be negatively related to such outcomes.
Methods: 124 METH dependent patients (49 females, M age=33.20 years) enrolled in community or correction treatment sites in Eastern Nebraska completed survey/interview measures of: risk factors (physical, emotional, sexual trauma; perceived stress, emotional coping), protective factors (social support, religiousness, altruism, problem focused coping, empathic concern), and METH-associated externalizing outcomes (hostility, somatization, interpersonal problems, drug severity, violent offenses).
Results: Correlational analyses showed general positive relations between emotional trauma, sexual trauma, perceived stress, and emotional coping, and interpersonal problems and drug severity. Further, there were significant negative relations between social support and drug severity (for EAs), religiousness and both hostility and interpersonal problems (for EAs), and empathic concern and hostility and violent offenses (for EAs). Problem focused coping and drug severity was positively related (for Latino/as).
Conclusions: Discussion will focus on the overall pattern of risk and protective factors across METH-dependent Latino/as and European Americans in the Northern Great Plains region.
Financial Support: Tobacco Settlement Funds (University of Nebraska-Lincoln) and a Health Disparities Grant (Center for Reducing Health Disparities, University of Nebraska Medical Center).

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COMT VAL/MET GENOTYPE ASSOCIATIONS WITH TREATMENT RESPONSE FROM A RANDOMIZED CLINICAL TRIAL OF CBT4CBT.

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Aims: COMT Val108/158Met polymorphism plays a role in addiction, but it has not been evaluated in terms of how it might affect response to validated behavioral therapies. Using data from a randomized trial evaluating computerized CBT (CBT4CBT) we evaluated treatment response and 6-month outcome by genotype.
Methods: 101 cocaine-dependent individuals were randomized to standard methadone maintenance treatment or standard treatment plus CBT4CBT. Complete 6-month data were available from 92% of the sample. Analyses indicated significant effects for CBT4CBT in terms of continuous abstinence as well as sustained effects through follow-up. 81 of 101 subjects contributed genetic data.
Results: 17 participants were classified as MET/MET type; the remainder as Met/Val or Val/Val. The sample was 64% female, 28% African American, and 10% Hispanic, with no significant differences by treatment or genotype. There was a genotype by time effect (F=4.0, p=.047), indicating greater decrease in cocaine use over time for the Met/Val/Val genotypes relative to Met/Met from baseline to the 6-month follow-up. There was a significant treatment condition by genotype interaction, suggesting less cocaine use among individuals with the Met/Val/Val subtypes when assigned to CBT4CBT versus standard methadone treatment (F=5.8, p=.02). A similar pattern was seen for neuropsychological indicators of cognitive control (emotional Stroop) suggesting individuals assigned to CBT4CBT had less interference from drug words compared with those assigned to standard methadone.
Conclusions: These are to our knowledge the first data linking COMT polymorphism to response to a specific behavioral therapy, where individuals with the Met/Val or Val/Val genotypes appeared to respond better to CBT as compared with standard treatment. As COMT polymorphism has been linked to aspects of cognition also linked to addiction, and CBT targets development of cognitive control, these data suggest differential treatment response linked to putative mechanisms of CBT effects.
Financial Support: Supported by NIDA grants R01/37-DA 015969 and P50-DA09241

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BINGE-LIKE ETHANOL CONSUMPTION IN C57BL/6J MICE PROMOTES SITE-SPECIFIC INCREASES OF INTERLEUKIN-1β EXPRESSION IN THE AREA OF THE AMYGDALA.

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Aims: Research in the neuroimmune field has found integral roles for the cytokine, IL-1β, in anxiety, stress, memory, and sickness behaviors, but few studies have attempted to link the role of IL-1β specifically to the modulation of ethanol consumption. This study examined the role of brain IL-1β in excessive binge-like ethanol drinking in C57BL/6J mice, by assessing IL-1β expression in key brain regions previously implicated in alcohol consumption studies.
Methods: Mice were exposed to a 4 day "drinking in the dark" (DID) binge-like ethanol consumption procedure, which promotes high ethanol intakes with associate blood ethanol concentrations in excess of 80 mg/dl (Sparta et al., 2008; Lowery et al., 2010). Brain tissue was collected via cylindrical punches of the hypothalamus and amygdala, and subsequently processed for real-time qRT-PCR. Gene expression was quantified for both the target (IL-1β) and housekeeping gene (β-Actin).
Results: In separate replications, binge-like ethanol drinking was compared to either a water drinking control group or a sucrose drinking control. In both experiments, mice with a history of binge-like ethanol drinking exhibited a significant increase of IL-1β mRNA in the amygdala ($p < 0.05$). Importantly, there were no differences in the expression of the housekeeping gene β-Actin between groups ($p > 0.05$). Furthermore, the hypothalamus did not show significant differences in IL-1β expression between water, sucrose, and ethanol drinking animals suggesting that ethanol-induced alterations of IL-1β mRNA are specific to certain brain regions ($p > 0.05$).
Conclusions: In conclusion, these data show that in mice exhibiting binge-like levels of ethanol consumption, IL-1β mRNA is significantly elevated in the amygdala, a brain region that has previously been implicated in modulating binge-like ethanol drinking in C57BL/6J mice.
Financial Support: NIDA & NIAAA funding
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INCREASING THE VALUE OF AN ALTERNATIVE MONETARY REINFORCER REDUCES CIGARETTE CHOICE IN ADOLESCENTS.

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Aims: Smoking can be conceptualized as an operant behavior. Changing the magnitude and availability of alternative reinforcers should shift behavior away from smoking. Adults' smoking behavior is sensitive to the magnitude and availability of alternative reinforcers; however, the extent to which the same is true for teens has not yet been shown in the laboratory. Compared to adults, adolescents tend to smoke fewer cigarettes per day, smoke more intermittently and have shorter smoking histories; therefore, results obtained with adult smokers may not always generalize to adolescent smokers.
Methods: To test the sensitivity of adolescent smoking choice to changes in the magnitude of alternative reinforcement, we gave adolescents ($N = 85$; $M = 16.45$ years old, $SD = 1.415$) the opportunity to make 20 choices between 2 puffs of their usual-brand cigarette or money following overnight abstinence. The magnitude of the monetary reinforcer varied across sessions in counterbalanced order ($0.00, $0.10, and $0.50).
Results: Results indicated that adolescents' choices for puffs decreased as a function of increasing monetary reinforcer magnitude, while money choices increased. A repeated-measures analysis of variance confirmed that mean choices for puffs were significantly different across monetary amount ($F(2,107)= 40.91$, $p < .0005$). Paired t-tests revealed that mean choices for puffs when money value was $0.00 significantly differed from means puffs when the money value was $0.10 ($t(85)=3.189$, $p=.002$) as well when it was $0.50 ($t(85)=8.427$, $p< .0005$). Mean choices for puffs also differed significantly when the value was $0.10 versus when it was $0.50 ($t(85)=6.090$, $p< .0005$).
Conclusions: These results extend previous laboratory work on the relationship between alternative reinforcers and cigarette choice to adolescents, and demonstrate that adolescent smoking behavior is sensitive to changes in the magnitude of concurrently available monetary reinforcers. These results have implications for behavioral treatments such as contingency management.
Financial Support: NIDA grants T32 DA016184 and R01 DA16737

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EVALUATION OF AN ADF PRODUCT'S ROUTE-OF-ADMINISTRATION PROFILE.

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Aims: Assessing the impact on abuse patterns of the introduction of abuse deterrent opioid formulations (ADFs) has focused, in part, on comparisons of the ADF's route of administration (ROA) profile with its baseline profile prior to ADF introduction. However, the routes that abusers use may be influenced by several factors, including continued availability of the original formulation and availability of non-ADF products as alternatives for abuse, particularly generic versions of the parent drug. A simple pre-post comparison of ROA profiles assumes that abuse of the original product would remain unchanged in the time period following introduction of the ADF. To examine this assumption, we reviewed ROA patterns for both original and reformulated extended-release (ER) oxymorphone, and generics after introduction of crush-resistant ER oxymorphone.
Methods: ROA data from Q4 2012 through Q3 2013 were examined among adults assessed for substance abuse problems using the NAVIPPRO® Addiction Severity Index-Multimedia Version (ASI-MV®). The ASI-MV is a computer-administered, clinical interview that collects self-report data from adults on past 30-day drug abuse, including prescription opioids. ASI-MV respondents differentiate abuse of prescription products using screen images.
Results: Among abusers of the product, the ROA profile for the original oxymorphone ER historically revealed high levels of snorting (76%) and low injection (19%). In the last year, the reformulated ER oxymorphone showed low levels of snorting (20%), but higher injection (62%). However, currently, abusers of original ER oxymorphone report continued snorting (60%) but greater injection (38%) than observed historically. The ROA profile for non-ADF generic versions are more often snorted (72%) and injected (32%).
Conclusions: ROA profiles for oxymorphone ER products change over time. Understanding the public health impact of ADFs must take into account this dynamic process as new products enter the market such as higher-dose, non-ADF generic versions. Data updated through Q1 2014 will be presented.
Financial Support: Inflexxion, Inc. and Endo Pharmaceuticals Inc.

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"IT'S LIKE TRYING TO CHANGE A FLAT TIRE WHEN YOU GOT A BLOWN ENGINE." COUNSELOR VIEWS ON TREATING CLIENTS WITH CO-OCCURRING MEDICAL CONDITIONS.

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Aims: Aims: While the integration of substance abuse screening and intervention into primary care has been central to the Affordable Care Act, medical problems in clients entering substance use disorder (SUD) treatment has received less attention. Individuals' entering SUD treatment often present with medical co-morbidities, but little is known about how they impact SUD counseling. Study aims were to: a) describe SUD counselor experiences treating patients with medical co-morbidities; b) explore counselor perceptions of the relationship between SUDs and medical issues; c) identify challenges in providing treatment to such clients; and d) identify strategies used to assist their clients.
Methods: Methods: The present study used an Interpretative Phenomenological Analysis to explore community outpatient counselors' experiences treating clients with medical issues. In-depth interviews were completed in Summer, 2013, with 5 SUD treatment counselors in Central Virginia. The interviews were analyzed in Atlas-ti qualitative software and themes compared across interviews.
Results: Results: Four super-ordinate themes emerged illustrating the relationship between SUDs, medical conditions and other bio-psychosocial factors. Analyses highlight how SUD outpatient counselors assist clients in focusing on therapy, identifying resources to treat the basic needs of clients (including medical care) and the challenges brought on by limited resources, complex systems, and client fear. Also prominent were unique challenges related to medical conditions treated by potentially habit forming medications and traumatic brain injury. SUD counselors also advocated for additional education in: counselor self-care, trauma, grief and loss, chronic pain and assessment.
Conclusions: Conclusion: Study findings support the need for additional research and multi-disciplinary discussion focused on integrated behavioral and physical health care.
Financial Support: Financial Support: 2U10 DA013034

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A LATENT CLASS ANALYSIS OF TRAUMATIC EVENTS EXPERIENCED BY DRUG USERS AND THEIR PARTNERS: ASSOCIATIONS BETWEEN DISTINCT TRAUMA PATTERNS AND PSYCHIATRIC AND SUBSTANCE USE DISORDERS, SEX TRADE, AND SEXUALLY TRANSMITTED INFECTIONS.

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Aims: Many individuals experience multiple traumatic events (TEs), but few studies have examined the heterogeneity of TEs and associated problems including substance use disorders (SUDs). Such studies are needed in order to inform interventions for subpopulations of trauma victims most at risk for specific problems. This study examined the heterogeneity of TEs and associations between distinct patterns of TEs and various problems including SUDs among high-risk adults.
Methods: Participants were 281 adults who recently used drugs and were HIV negative (index participant) or were the intimate partners of index participants. Latent class analysis was used to examine the heterogeneity of the following lifetime TEs: 1) childhood physical or sexual abuse, 2) adult unwanted sex involving threat or use of force, 3) adult physically or otherwise abusive relationship, 4) danger of serious injury or death, or 5) other TEs. The class profiles of the optimal LCA model were tested to see whether they differed in their prevalence of psychiatric disorders, SUDs, sex trade, and sexually transmitted infections after controlling for age and gender.
Results: The majority of the sample was female (58.7%) and used drugs in the past six months (68%). The best fitting model consisted of three classes, which were characterized by the following probabilities: moderate other TEs (Class 1: 36.4%), high injury and other TEs (Class 2: 26.4%), and high adult abusive relationship and other TEs (Class 3: 35.2%). Class 3 was associated with the greatest prevalence of problems studied except SUDs, which tended to be more prevalent in Class 2.
Conclusions: These preliminary findings warrant replication in larger samples. Implications for preventions and interventions will be discussed.
Financial Support: This study was funded by a grant (R01DA014498) from the National Institute of Drug Abuse.

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MONITORING MARIJUANA USE AND RISK PERCEPTIONS WITH GOOGLE TRENDS DATA.

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Aims: Monitoring marijuana use at a population-level can be important for understanding potential consequences of the current shift in the marijuana policy landscape. Google Trends data is a keyword research tool that provides near real-time search query trend data based on Google searches and has potential to monitor important public health events in near real-time. In the present study, we validate Google Trends data for tracking marijuana use and risk perceptions of marijuana use in near real-time.
Methods: We compared 2011 Google Trends relative search volume data for marijuana with state prevalence of youth (grades 9-12) and adult (age 18 and older) marijuana use and perceptions of risk for smoking marijuana using data from the 2010-2011 United States National Survey on Drug Use and Health (NSDUH). We used the Pearson correlation coefficient to measure the associations.
Results: We found significant positive correlations between state Google Trends marijuana relative search volume and current marijuana use among youth ($r=0.50$, $p<.001$) and adults ($r=0.59$, $p<.001$). Likewise, there was a moderate positive correlation between Google Trends relative search volume and believing that occasional marijuana use is not of great risk ($r=0.54$, $p<.001$ among youth and $r=0.51$, $p<.001$ among adults).
Conclusions: Google Trends data are free, easy-to-use, and readily available; we validate Google Trends data as a valuable resource for tracking marijuana use behaviors and attitudes towards marijuana use in near real-time.
Financial Support: This publication was made possible by Grant Numbers UL1 RR024992 and KL2 RR024994 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research and by K02DA021237 from the NIH. Other support includes an NIH Career Development Award awarded to Dr. Cavazos-Rehg (NIDA, K01DA025733) and NIDA, R01 DA032843, an NIH Midcareer Investigator Award awarded to Dr. Bierut (K02 DA021237), R01 DA031288 awarded to Dr. Grucza.

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SUBSTANCE USE, MENTAL HEALTH AND INCARCERATION AMONG MEXICAN-AMERICAN YOUNG ADULT MEN WITH A HISTORY OF GANG MEMBERSHIP.

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Aims: Hispanics represent 13 percent of the United States population yet make up almost 20 percent of individuals incarcerated. Despite this, few studies have examined the long term comorbid conditions (drug use and mental health) of young adult male Hispanic populations with a history of serial incarceration. The present study examines variations in substance use and mental health conditions (Brief Symptom Inventory), among a street recruited sample of Mexican American young men with histories of incarceration.
Methods: Data come from an on-going NIDA funded longitudinal study of a cohort of 275 adolescent gang members initially interviewed over 15 years in San Antonio, Texas.
Results: Data observed significant and positive associations between past year heroin use and current mental health conditions (BSI severity, symptoms and individual outcomes). Data further reveal current heroin users as having a higher average number of past incarceration episodes than nonusers ($\beta = .03$, $p<.05$). With regards to total number of years incarcerated, a negative association is observed such that those who are current users have, on average, shorter lengths of time spent incarcerated over their lifetime ($\beta = .20$, $p<.001$).
Conclusions: Discussed are the distinct mechanisms by which imprisonment influences substance use and mental health conditions among this minority population. The identification of these co-occurring conditions may contribute to the development of appropriate drug use interventions that may curtail negative health trajectories for these young men.
Financial Support: This research is supported by a NIDA funded grant 7R01DA023857.

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POST-INCARCERATION FACTORS AND RELAPSE TO OPIOID INJECTION IN ST. PETERSBURG, RUSSIA.

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Aims: To measure the association between risk environment factors and the elapsed time to relapse to injection opioids after release from incarceration among a sample of active injection drug users (IDUs).
Methods: 811 IDUs were recruited into a cross-sectional study in St. Petersburg, Russia from September 2012 – June 2013 by respondent driven sampling. This analysis focuses on the IDUs who reported ever being incarcerated. We used logistic regression to model the outcome of relapsing to injection opioid use within 2 weeks of release. Predictors included the physical, social, economic, and political risk environment and their association to quick relapse.
Results: Among the 274 IDUs who reported having been incarcerated, 236 (86%) were men, and were significantly older and more likely to be HIV-positive than those who had never been incarcerated (p-value <0.0001, 0.0005 respectively). Almost half (n=129) relapsed within 2 weeks of release. In the multivariate logistic regression, IDUs who were not employed at the moment of relapse were 23.15 (95% CI 9.76, 58.94) times as likely to have relapsed quickly. Also, those who injected in prison and had not received services from a syringe exchange program were 4.04 (95% CI 1.71, 9.53) and 7.44 (95% CI 2.72, 20.32) times as likely to have relapsed shortly after release. All alcohol covariates were associated with an increased odds of relapsing within 2 weeks, however recent alcohol use was the strongest predictor in the model. For every drink consumed in the past week the odds of relapsing within two weeks increased by 1.06 fold (95% CI 1.03, 1.08).
Conclusions: Almost half of IDUs relapsed to injection opioids within 2 weeks of release, suggesting that many are at high risk of death and non-fatal opioid overdose. In addition to medical care, post-release interventions should focus on strengthening linkage to social services, such as aiding with employment and reducing alcohol consumption.
Financial Support: Funding for this research was supported by the NIDA(F31DA035709 for JAC and 5R01DA02988804 for RH), NIMH (5T32MH02003115 and CIRA (2P30MH06229411).

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PAST YEAR NON-MEDICAL OPIOID USE AND PTSD DIAGNOSIS: INTERACTIONS WITH GENDER AND ASSOCIATIONS WITH SYMPTOM CLUSTERS.

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Aims: The purpose of this study is to examine associations between PTSD (diagnosis and specific symptom clusters) and past year nonmedical opioid use (NMOU), as well as differences by gender.
Methods: Data from the National Epidemiologic Survey on Alcohol and Related Conditions Wave 2 (N=34,653) were used to examine associations between past year PTSD diagnosis and past year NMOU. Selecting for those with a PTSD diagnosis (N=2,492), associations between symptom clusters (hyper-arousal, avoidance, re-experiencing, emotional numbing; standardized variables) and NMOU, as well as gender interactions, were explored. Models accounted for survey design and were adjusted for age, education, race/ethnicity, and pain.
Results: In bivariate analyses, PTSD diagnosis and all symptom clusters were positively associated with past year NMOU for both men and women. In adjusted models, PTSD diagnosis was positively associated with NMOU for both men and women; the odds ratio for women was slightly larger (Women: OR=1.23, 95%CI=1.95, 2.66; Men: OR=1.65, 95%CI=1.37, 2.00, $p<0.01$). There were significant gender interactions with hyper-arousal and avoidance symptom clusters. Hyper-arousal was positively associated with NMOU for men (OR=1.84, 95%CI =1.50, 2.25) but not women, while avoidance was positively associated with NMOU for women (OR=1.23, 95%CI=1.03, 1.47) but not men. Emotional numbing and re-experiencing symptoms were not associated with NMOU ($p > 0.05$).
Conclusions: These results illustrate significant associations with NMOU and PTSD diagnosis as well as gender interactions with PTSD symptom clusters and NMOU. The findings have substantial implications for NMOU screening among individuals diagnosed with PTSD; further work is needed to better understand causative factors and temporal associations.
Financial Support: R01DA034072(GGH); T32MH01423539(PHS trainee)

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WITHDRAWN

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WITHDRAWN

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PARENT-TEEN DRUG USE DISCUSSIONS: ASSOCIATIONS WITH SUBSTANCE USE.

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Aims: Although talking to teens about drugs is often recommended to parents, we know little about how parents actually discuss drugs with their children. This study examined observed parental drug advice during parent-adolescent discussions. Based on findings from parent reports of drug use advice (Chassin et al., 1998), we hypothesized that observed advice involving stating rules against drugs and discussing drug scenarios and consequences would be associated with lower adolescent physiological arousal and substance use.
Methods: Fifty eight 12-17 year olds and their parents discussed the topic of alcohol and/or drugs for ten minutes. The discussions were videotaped and coded for drug use advice (stating rules against drug use, discussing scenarios [e.g., what would you do if you were offered alcohol?], discussing consequences) and parenting (warmth, negative parenting). Inter-rater reliability was good, ave ICC = .81. Before, during, and after the discussions, adolescents' heart rate (HR), blood pressure (BP), and salivary cortisol levels were assessed. Youth reported use of substances on the YRBS.
Results: Regular and logistic regressions were conducted predicting physiological responses and substance use (yes/no). Findings showed that parental discussion of scenarios was associated with lower adolescent BP responses ($\beta = -.33$, $p < .05$) and lower substance use (Exp[B] = .59, $p < .05$). Statements of rules against drug use were associated with higher HR and BP responses (β's = .26-.30, p's < .05) and greater substance use (Exp[B] = 2.40, $p < .05$). Negative parenting was associated with higher cortisol responses ($\beta = .29$, $p < .05$).
Conclusions: Drug use advice involving discussion of scenarios and fewer statements of rules against drugs and criticism was associated with lower arousal and substance use in youth. Findings suggest that interventions encourage parents to discuss scenarios rather than focus on rules against drugs.
Financial Support: Supported by: NIH (K01-DA-024759, UL1-DE19586), ABMRF, and AACAP grants.

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GREATER EXPOSURE TO STRESSORS DURING PREADOLESCENCE PREDICTS EARLY ADOLESCENT SUBSTANCE USE.

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Aims: Adolescents with a family history of alcohol and other drug use disorders (FH+) are at increased risk for developing substance use disorders relative to those without such histories (FH-). One mechanism that may contribute to this risk is exposure to stressors. FH+ individuals report experiencing more lifetime stressors and exposure to stressors is associated with the development of substance use disorders. However, there is limited research on exposure to stressors in FH+ individuals during preadolescence, prior to the adolescent spike in substance use initiation.
Aim: To quantify stressors reported over a 1 year period in preadolescence among FH+ youth who later initiated substance use, and compare this to FH+ and FH- adolescents who did not initiate use.
Methods: As part of an ongoing longitudinal study, self-reported stressors during preadolescence were compared in 43 FH+ youth who initiated substance use in early adolescence and demographically matched FH+ (n=40) and FH- adolescents (n=39) who did not initiate substance use. Exposure to stressors was assessed using the Stressful Life Events Schedule, a standardized semi-structured interview, at study entry (M age = 11.2 years, SD = .78) and 6 and 12 month follow-ups.
Results: Participants who initiated substance use during early adolescence reported significantly greater lifetime exposure to stressors at study entry and a relatively greater increase in stressors over a 1 year period in preadolescence, compared to both FH+ and FH- non-users. FH+ non-users reported more stressors at study entry than did FH- non-users, but these groups did not differ in their exposure to stressors over the 1-year follow-up.
Conclusions: FH+ adolescents who initiated substance use had greater stress exposure in preadolescence. As part of our ongoing longitudinal studies, we will examine how stressors during pre- and early adolescence influence the development of substance use and substance use disorders.
Financial Support: National Institutes of Health (R01-DA026868, R01-DA033997, T32 DA031115)

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PATTERNS OF CONCURRENT SUBSTANCE USE AMONG PRESCRIPTION STIMULANT MISUSERS: RESULTS FROM THE NATIONAL SURVEY ON DRUG USE AND HEALTH.

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Aims: To examine patterns of concurrent substance use among adults who used prescription stimulants non-medically.
Methods: We used latent class analysis (LCA) to examine patterns of past-year problematic substance (i.e. had any criteria of abuse or dependence) in a sample of 6,244 adult participants of NSDUH 2006-2011 who reported past-year non-medical use of prescription stimulants. Multivariate latent regression was used to determine the association of socio-demographics, mental health and deviant behavior characteristics with the latent classes.
Results: A four class model had the best model fit. The largest class was comprised of individuals with low probabilities of any problematic substance use (Low substance users, 49.1%); the smallest class was comprised of individuals with high probabilities of problematic use of multiple drugs and alcohol (Polysubstance users, 5.3%). A third class was comprised of those who were problematic users of all types of prescription drugs (Prescription drug users, 11.8%). A fourth class included participants with high probabilities of problematic alcohol and marijuana use (33.8%). Regression results showed that Prescription drug users and Polysubstance users were more likely to report past-year mental health problems, deviant behaviors, and mental or substance treatment use, while Alcohol/marijuana users reported more deviant behaviors and substance treatment use, compared to Low substance users.
Conclusions: Nonmedical users of prescription stimulants are a heterogeneous group, with a large subgroup rarely having any substance problems. These subgroups have distinct patterns of mental health comorbidity, behavior problems and service use, which can offer implications for prevention and treatment of nonmedical stimulant use.
Financial Support: DA023186

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STATISTICAL ASSESSMENT FOR ABUSE DETERRENT FORMULATION IN CLINICAL ABUSE POTENTIAL STUDIES.

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Aims: Abuse and misuse of prescription opioid analgesics is a serious and growing public health problem. Consequently, the development of abuse-deterrent formulations (ADF) that are less prone to misuse or abuse is a public health priority. In recent years, there is increased interest by the Pharmaceutical Industry in developing ADF Schedule II opioid drugs, including crush resistance. In January of 2013, FDA published "FDA Guidance for Industry: Abuse Deterrent Opioids-evaluation and labeling". Since then many questions are raised on statistical evaluations for ADF in clinical abuse potential studies. In this presentation, I will discuss the statistical issues related to ADF assessment.
Methods: The 2013 FDA guidance suggests evaluating mean difference in Emax between ADF and its control as primary analysis. The guidance also suggests using either responder analysis or analysis of the median percent reduction in the secondary analysis. These analyses include unknown abuse deterrent margin, unknown definition of a responder, and unknown percent deterrent reduction. These unknown parameters bring great difficulties on conducting the statistical analyses for assessing abuse deterrent effect of the ADF. In this presentation, I will present the issues related to these methodologies, relationships among these methodologies, and then propose potential solutions to resolve the difficulties. The presentation will also urge to let more statisticians get involved in this research area.
Results: This presentation will provide the audience with the details of the FDA guidance on statistical analyses in clinical abuse potential studies for ADF, list the issues related to each methodology, and show the links among these methodologies as well as bring attention to the audience that more statisticians should get involved in conducting research in this area.
Conclusions: Both the primary analysis on Emaxs using the mean difference (or median difference) and the analysis on percent reductions are important for evaluating ADF.
Financial Support: N/A

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ASSOCIATION BETWEEN AGE, SUBSTANCE USE AND HEALTH SERVICE USE IN MEDICARE ELDERLY PROSTATE CANCER PATIENTS.

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Aims: To analyze the age specific variation in prevalence of substance use and its effects on health service use in Medicare elderly with advanced prostate cancer.
Methods: SEER-Medicare linked database between 2000 and 2009. From a cohort of men diagnosed with advanced prostate cancer between 2001 and 2004, we identified those with a diagnosis of substance use (ICD-9 codes: Alcohol dependence syndrome-303.xx, Drug dependence 304.xx and Non-dependent abuse of drugs 305.xx). Age was categorized as 66-75 years and >75 years. The year post-diagnosis of prostate cancer was treatment phase. We compared the prevalence of substance use and health inpatient, outpatient and ER service utilization across two age groups.
Results: Of the 14,277 elderly with advanced prostate cancer, 64% were aged 66-75 years and 26% were >75 years. Prevalence of substance use was higher in the 66-75 years group, compared to the >75 years group (12.5% vs. 7.0%, p=0.0381). Within age group comparison showed that for both age groups, those with substance use had higher health service use, compared to those without. Between age group comparison indicated significant variations in health services use. The 66-75 years group had higher inpatient service use (28% vs. 12%, p=0.0346) and higher ER use (74% vs. 58%, p=0.0261), compared to the >75 years group. Outpatient use was comparable across both age groups.
Conclusions: Substance use is an important psychosocial co-morbidity in elderly cancer patients. Our results indicate age specific variation in the intersection of cancer and substance use in Medicare elderly with advanced prostate cancer. As prostate cancer incidence increases exponentially with older age, a surge in older prostate cancer patients will pose a challenge to the healthcare system. Thus, tailored strategies to screen and treat substance use in elderly prostate cancer patients are essential.
Financial Support: Department of Defense Hypothesis Development Grant # W81XWH-12-1-0089 PC110707 and National Institute on Aging, National Institutes of Health-Grant # R21AG034870-01A1

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TRENDS IN ABUSE AND DIVERSION IN MULTIPLE SURVEILLANCE SYSTEMS THREE YEARS AFTER INTRODUCTION OF REFORMULATED OXYCONTIN.

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Aims: In August 2010, Purdue Pharma introduced reformulated OxyContin intended to deter abuse through snorting or injecting. Previous findings showed declines in abuse and diversion across multiple surveillance systems in the first 2 years after reformulation. This study extends these findings to 3 years and beyond.
Methods: Quarterly data from four on-going major surveillance systems were examined: 1) Intentional abuse exposures in the RADARS® System Poison Center (PC) program and 2) National Poison Data System (NPDS); 3) Assessment of individuals in substance abuse treatment through the NAVIPPRO ASI-MV system and 4) reports by law enforcement officials participating in the RADARS System Drug Diversion program.
Results: Population-adjusted rates of intentional abuse exposures for OxyContin reported in the RADARS PC program and NPDS declined 42% and 40%, respectively, in the second year after reformulation (Jul 2011-Jun 2012) compared to the year prior to reformulation (Jul 2009-Jun 2010) and these declines increased to over 50% in the third year post-reformulation (Jul 2012-Jun 2013). OxyContin drug diversion rates declined 57% in the second year and declined 72% in the third year after compared to the year before reformulation. Among opioid abusers assessed in the NAVIPPRO system, rates of abuse of reformulated OxyContin remained relatively steady in the post-reformulation period through Mar 2013 at approximately 50% lower than rates for original OxyContin in the 14 months prior to reformulation. In all surveillance systems, the reductions in rates of abuse were larger for OxyContin than comparator opioids. For those studies that assessed route of administration for abuse (PC studies and NAVIPPRO), declines in abuse were larger for non-oral than oral routes.
Conclusions: These findings indicate that declines in abuse of OxyContin after reformulation have persisted up to three years post-reformulation. Additional follow-up is needed to assess whether these trends continue.
Financial Support: Research funded by Purdue Pharma, L.P.

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"DESTINED FOR SUCCESS"? BRAIN RESPONSES DURING DRUG CUE EXPOSURE FORETELL CLINICAL OUTCOME IN COCAINE PATIENTS.

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Aims: Against very harsh odds, subgroups of addicted individuals succeed in avoiding relapse. We hypothesized that these individuals have a profile of brain responses that help them to manage the "pull" of relapse-provoking drug cues. As compared to their unsuccessful counterparts, we predicted that patients "Destined for Success" would show either 1) "less GO!" (reduced response in nodes of the mesolimbic reward circuitry), 2) "more STOP!" (increased response in prefrontal modulatory circuits), or both, when exposed to visible drug cues.
Methods: We used event-related BOLD fMRI at 3 Tesla to measure the brain response to cocaine vs. neutral pictures of 500 msec duration in a group of cocaine inpatients later discharged into outpatient treatment with twice-weekly urine monitoring. Imaging data were pre-processed within SPM 8 for pre-planned contrasts (e.g., cocaine v. neutral cues), and then compared between two distinct outcome phenotypes for Weeks 1-3: patients "Destined for Success" (0 or 1 cocaine + urine; n=7) vs. those facing a "Rough Road Ahead" (5 or 6 cocaine + urines; n=9).
Results: As predicted, cocaine patients "Destined for Success" had reduced brain response to visible cocaine cues in two "GO!" regions, the VTA and the v. striatum – and increased brain response in two prefrontal modulatory "STOP!" regions, the lateral orbitofrontal cortex (LOFC) and the dorsomedial prefrontal cortex (dmPFC) (all $2>t<5$; $p<0.05$ uncor). "Destined for Success" patients also completed the 12-week trial in drug-free state.
Conclusions: Individual differences in the brain response to drug cues may indeed contribute to relapse vulnerability. Treatments targeting the brain's "GO!" and "STOP!" circuitry will determine whether the pattern of activity in these circuits can be altered, increasing the number of individuals "destined for success."
Financial Support: Support: Commonwealth of Pennsylvania CURE Addiction Center of Excellence; NIH/NIDA (T32DA028874; P5012756); VA VISN 4 MIRECC.

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ATTITUDES TOWARD COMPUTER INTERVENTIONS FOR PARTNER ABUSE AND DRUG USE AMONG WOMEN IN THE EMERGENCY DEPARTMENT.

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Aims: The aims of this study were to explore womens' attitudes about use of computers for screening and intervening in drug use and partner abuse.
Methods: Seventeen adult women with recent histories of partner abuse and drug use were recruited from an urban ED to participate in one-on-one semi-structured interviews. A coding classification scheme was developed and applied to the transcripts by two independent coders. The research team collaboratively decided upon a thematic framework and selected illustrative quotes.
Results: Most participants used computers and/or mobile phones frequently and reported high self-efficacy with them. Women described emotional difficulty and shame around partner abuse experiences and drug use; however, they felt that reporting drug use and partner abuse was easier and safer through a computer than face-to-face with a person, and that advice from a computer about drug use or partner abuse was acceptable and accessible. Some had very positive experiences completing screening assessments. However, participants were skeptical of a computer's ability to give empathy, emotional support or meaningful feedback. The ED was felt to be an appropriate venue for such programs, as long as they were private and did not supersede clinical care.
Conclusions: Women with partner abuse and drug use histories were receptive to computerized screening and advice, while still expressing a need for the empathy and compassion of a human interaction within an intervention.
Financial Support: This work is supported by a K23 career development award from the National Institutes of Drug Abuse (K23 DA031881).

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THE ROLE OF GLUTAMATE ON INCENTIVE VALUE ATTRIBUTION: ACQUISITION AND EXPRESSION.

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Aims: Using preclinical models, a growing literature indicates that individuals that attribute incentive value to reward-predictive stimuli and exhibit sign-tracking behavior are more sensitive to drug reward. Reward-predictive stimuli play a large role in controlling drug-seeking behavior, but the neurobehavioral mechanisms underlying how a stimulus gains incentive value are largely unknown.
Methods: To determine the role of NMDA signaling in the acquisition of incentive value to reward associated stimuli, 12 Sprague Dawley rats were trained on a Pavlovian conditioned approach (PCA) task, where rats were pseudo-randomly presented with either a lever or a tone followed by non-contingent food delivery, for 14 days with pretreatments of saline or MK-801. Another set of 12 Sprague Dawley rats were trained on the same PCA task as above and switched to a choice procedure; this choice procedure used 5 blocks of choice trials, where a response on an illuminated nosepoke produced the previously conditioned lever or tone, both followed by food. Additionally, the probability of food following the lever CS was decreased over the 5 choice blocks. Following stable performance, animals were then pretreated with MK-801 or saline prior to choice sessions.
Results: Mixed-factors ANOVA indicated animals pretreated with MK-801 did not attribute incentive value towards the lever during PCA acquisition. For the choice procedure, hyperbolic model fits were used to examine choice functions, and these fits indicated that when the probability of food reinforcement was equivalent across both stimuli, an exclusive preference for the lever CS was observed. Furthermore, as the probability of food following the lever decreased, preference for the lever decreased. Finally, administration of MK-801 prior to choice sessions shifted the choice functions.
Conclusions: Collectively, these results indicate glutamate is required for the attribution of incentive value attribution to reward-associated stimuli, suggesting that the relationship between glutamate signaling and incentive value attribution may underlie cue-induced relapse.
Financial Support: NIH K99 DA033373

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A SYSTEMATIC REVIEW OF COMMUNITY OPIOID OVERDOSE PREVENTION AND NALOXONE DISTRIBUTION PROGRAMS.

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Aims: To describe the current state of the literature on Opioid Overdose Prevention Programs with particular focus on the effectiveness of these programs. This review synthesizes demographic and clinical characteristics of OOPP participants to answer the following questions: 1) Do OOPPs with naloxone distribution reduce fatal and non-fatal overdose rates among participants, 2) Are OOPPs effective at increasing non-medical bystander knowledge of prevention, risk factors, and recognition of opioid overdose, and 3) Do non-medical bystanders trained at OOPPs respond correctly to witnessed opioid overdoses?
Methods: An interdisciplinary team of researchers used systematic search criteria to identify relevant articles, which were abstracted and assigned a quality assessment score. Nineteen articles evaluating OOPPs met the search criteria for this systematic review.
Results: Principle findings included participant demographics, percent survival in overdose victims receiving naloxone, post-naloxone outcome measures, opioid overdose prevention program characteristics, changes in knowledge pertaining to overdose responses and barriers to naloxone administration during overdose responses. Naloxone was used successfully administered 1,949 in 18 of the 19 studies and there was some evidence that training is associated with an increase in knowledge when responding to overdose events.
Conclusions: The current evidence from non-randomized studies suggests that bystanders (mostly opioid users) can and will use naloxone to reverse opioid overdoses when properly trained, and that this training can be done successfully through OOPPs. Further research, including cohort studies with active long-term follow-up as well as randomized trials of effectiveness, are needed.
Financial Support: None

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PERCEIVED DISCRIMINATION, DEPRESSIVE SYMPTOMS, AND SUBSTANCE USE AMONG AFRICAN-AMERICAN AND AFRO-CARIBBEAN YOUNG ADULTS.

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Aims: Perceived discrimination is an important health-related stressor. As suggested by the stress-coping model, people may turn to substance use as a means to reduce the negative effects of discrimination. This study examined how perceived discrimination and depressive symptoms are structurally related to lifetime and recent substance use among African American and Afro-Caribbean young adults.
Methods: Data from the National Survey of American Life-Adults were used. Respondents (n= 1,910) were between ages 18 and 35 years of age. Multiple-group structural equation modeling was used to evaluate model fit and test the hypothesized models.
Results: Results showed good fit of the hypothesized model in both African Americans and Afro-Caribbeans. Invariance of model fit was found across ethnicity. Mediation models explained a) 18.4% and 49.2% of the variance in lifetime substance use for African Americans and Afro Caribbeans, respectively, and b) 23.7% and 35.1% of the variance in recent substance use for African Americans and Afro Caribbeans, respectively. Mediation tests indicated that depressive symptoms partially mediated the relationship between discrimination and lifetime and recent substance use for African Americans. Depressive symptoms fully mediated the relationship between discrimination and lifetime substance use for Afro-Caribbeans. Depressive symptoms did not mediate the relationship between discrimination and recent substance use among Afro-Caribbeans. Depressive symptoms was not associated with recent substance use among Afro-Caribbeans.
Conclusions: Results of the study shed light on the influence of discrimination on substance use among African American and Afro-Caribbean young adults and suggest the importance of exploring within group differences in mechanisms of substance use.
Financial Support: This work was supported by funds from the AAUW and National Institutes of Health/National Institute on Drug Abuse (1K01DA035895-01) awarded to the first author.

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MEDICAID BUDGET IMPACT OF GENERIC BUPRENORPHINE / NALOXONE TABLET.

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Aims: The buprenorphine/naloxone (Bup/Nal)combination for the treatment of opioid dependence is available in two forms - sublingual film and tablet. Recent studies demonstrated that treatment with film leads to improved treatment retention and lower healthcare costs. In March 2013 generic tablets appeared on the market. A budget impact model was built to compare health care expenditures based on current market shares of Bup/Nal film and generic Bup/Nal tablet.
Methods: A Markov model was developed to track a cohort of opioid dependent patients treated with Bup/Nal film or Bup/Nal tablet through the following treatment phases: initiation, maintenance, discontinuation, off treatment and re-initiation. Model forecasts for year 1 through year 5. It is based on monthly cycles. Transition probabilities and costs of each phase were estimated based on MarketScan Medicaid research database for the period from September 2010 to June 2012. The total expenditure for the plan and expenditure per plan member per month were predicted over 5 years. Two market share scenarios were considered: 1) 67% of film and 33% of all generic tablets combined (includes: Amneal, Actavis, Malinkrodt and Orexo tablet based on market shares), and 2) 100% of film.
Results: In the 100% Bup/Nal film group (scenario #2), cost of outpatient care was 7.1% higher, which may indicate that patients treated with film have more medical follow-up. Cost of emergency and inpatient care in the Scenario #2 were lower by 7.9% and 12.1%, respectively. The latter was mostly driven by the 13% decrease in the cost of non-psychiatric inpatient care. Total costs for the US Medicaid program over five years were lower by 2.9%, or $82.3 million, for Scenario 2.
Conclusions: Treatment with buprenoprhine/naloxone film formulation results in higher costs of outpatient care. However, these effects are offset by a considerable decrease in the costs of emergency care and hospitalizations, which leads to the overall cost-savings to the Medicaid programme.
Financial Support: Study sponsored by Reckitt Benckiser.

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FAMILY, FRIEND, AND SIGNIFICANT OTHER SUPPORT AND HIV-RELATED DRUG AND SEX RISK PRIOR TO INCARCERATION AMONG AFRICAN-AMERICAN MEN IN PRISON.

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Aims: To evaluate the association between perceived support and HIV risk behaviors among African American men involved in the criminal justice system. We hypothesized that significant other support will offer the greatest protection against sex risk, while family support will offer the greatest protection against drug use.
Methods: Project DISRUPT is an ongoing cohort study of African American men being released from prison in NC who were in committed partnerships at the time of incarceration (N=173). During the baseline (in-prison) survey, three four-item scales assessed perceived levels of support from family, friends, and significant others during the six months prior to incarceration. Participants scoring equal to or above the median of the averaged scores on these scales were considered as having "high" levels of this type of support. We assessed associations between support and self-reported sexual risk behaviors and drug use in the six months before incarceration.
Results: Outcomes included pre-incarceration marijuana use (62%), crack/cocaine use (18%), ecstasy use (11%), multiple partnerships (44%), concurrent partnerships (33%), and sex trade (9%). In analyses adjusting for age, poverty, and depression, high levels of friendship support were associated with reductions in ecstasy use (AOR: 0.33, 95% CI: 0.11-0.99). High levels of significant other support were associated with protection against multiple partnerships (AOR: 0.28, 95% CI: 0.14-0.58) and sex trade (AOR: 0.16, 95% CI: 0.04-0.62).
Conclusions: Among incarcerated African American men, feeling supported by significant others may protect against some sexual risk behaviors, while feeling supported by friends may protect against use of some drugs.
Financial Support: NIDA R01DA028766.

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TRENDS IN CARE FOR PERSONS WHO INJECT DRUGS IN SAN FRANCISCO.

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Aims: Healthcare policy & practice changes in San Francisco over the past 10 years were intended to improve healthcare services for vulnerable persons including those who inject drugs (PWIDs; including universal healthcare & HIV treatment, expanded HIV testing & agonist maintenance services, availability of hepatitis C RNA testing, non-prescription pharmacy syringe sale, & lay distribution of naloxone). We analyzed local National HIV Behavioral Surveillance (NHBS) data for evidence of a secular trend in PWID health measures associated with these changes.
Methods: Data were from interviewer-administered surveys from 3 cross-sectional respondent-driven sampling (RDS) studies conducted in 2005, 2009 & 2012, including persons >=18 years who had injected illicit substances in the past year. RDSAT was used to calculate RDS weighted point estimates and differences considered significant if 95% CIs did not overlap.
Results: PWIDs in later cycles (2005, 2009, 2012 respectively) were more likely to have health coverage (38%, 57%, 83%), access syringes at pharmacies (18%, 34%, 32%), and access free condoms (61%, 59%, 81%). PWIDs were less likely to report an HIV test in the past 12 months (75%, 52%, 52%). There was no change in most measures of interest, including the proportion unaware of their HIV status, on anti-retroviral therapy, vaccinated for viral hepatitis, ever treated for hepatitis C, usually/always using a sterile syringe, having unprotected intercourse with serodiscordant partners, or entering drug or alcohol treatment.
Conclusions: We found evidence of improved access to syringes and health insurance consistent with interval policy changes, but not expected improvements in blood-borne virus screening or treatment. PWIDs in San Francisco remain unacceptably unaware of their HIV status (43% unaware) and with just 67% on ARVs, broadened treatment guidelines may not have impacted PWIDs as they have other populations. These findings suggest a need for a detailed assessment of PWID health and innovative interventions to improve disease screening and treatment.
Financial Support: Centers for Disease Control and Prevention

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DIFFERENCES BETWEEN RECENT QUITTERS AND CURRENT SMOKERS DURING PREGNANCY.

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Aims: The aim of this study was to investigate characteristics of and differences between women who quit smoking in early pregnancy ("recent quitters") and women who continue to smoke ("current smokers") through analysis of preliminary data from an ongoing randomized controlled trial.
Methods: Intake assessments were collected from pregnant women enrolled in a clinical trial investigating a phone-based intervention for postpartum smoking cessation and relapse prevention. Participants were classified as either current smokers or recent quitters based on self-report, and were contrasted on demographic and psychological variables utilizing ANOVA and logistic regression.
Results: Of the 123 participants, 38 (31%) were recent quitters and 83(69%) were current smokers at intake. Current smokers were more likely than recent quitters to report higher scores on measures of depression (p = 0.011); self-perceived stress (p =0.029); lifetime (p =0.008), past-year (p = 0.005), and past-month (p =0 .02) internalizing disorders; lifetime (p = 0.001) and past-year (p =0 .008) externalizing disorders, lifetime substance disorders (p = 0.017), and count of significant barriers to quitting smoking (p =0.018). Recent quitters were more likely than current smokers to report readiness to quit (93% vs. 74%, p =0.000), were more likely to have started smoking later in life (17.4 vs. 15. 1 years, p = 0.001) and more likely to report a higher count of motivations to quit (1.4 vs. 0.4, p =0.000). In logistic regression analysis only having a history of lifetime externalizing disorders (OR 0.55; 95% CI 0.31, 0.98]) and having past month tobacco dependence (OR 0.38; 95% CI0.19,0.75]) were significant predictors of quit status at intake.
Conclusions: Women who continue to smoke after learning they are pregnant differ from those who quit smoking. Smoking cessation interventions may be improved upon by assessing for mental health history and tobacco dependence as part of prenatal care.
Financial Support: Supported by NIDA grant #R34DA032683.

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EFFECTSOF THE DOPAMINE D3/D2 RECEPTOR ANTAGONIST BUSPIRONE ON FOOD/COCAINE CHOICE IN SOCIALLY HOUSED MALE CYNOMOLGUS MONKEYS.

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Aims: Dopamine D2-like receptors are prominently involved in mediating the abuse-related effects of cocaine. Accumulating evidence suggests that the D3 subtype represents an encouraging target for pharmacotherapies for cocaine abuse. In these experiments, we assessed the effects of the purported D3 receptor antagonist buspirone, administered by either the intravenous (i.v.) or oral (p.o.) route, on food/cocaine choice in socially housed male cynomolgus monkeys. The use of socially housed monkeys permits an assessment of whether the effects of buspirone are modulated by social variables. We have demonstrated that brain D2-like receptor availability and the behavioral effects of cocaine and other D2-like drugs are modulated by the social rank of the monkey.
Methods: Eight dominant- and nine subordinate-ranked monkeys served as subjects. Monkeys self-administered cocaine under a concurrent fixed-ratio schedule in which they chose between a food pellet and a cocaine injection (0.0, 0.003, 0.01, 0.03, 0.1 mg/kg per injection in consecutive components, with 10 total reinforcers per component). When cocaine choice was stable, subgroups of dominant and subordinate monkeys (n≥6) received buspirone i.v. (0.03-0.56 mg/kg, 3 minutes before the behavioral session) or p.o. (3.0-17.8 mg/kg, 45 minutes pre-session). The dependent variables of interest were percent cocaine choice, and the number of cocaine and food choices in each component.
Results: Buspirone was 10 times more potent via the i.v. route. Both i.v. and p.o. buspirone decreased cocaine choice in most dominant monkeys (4/6); however, few subordinates (2/7) were affected when buspirone was given by either route.
Conclusions: Taken together, the data suggest that effects of buspirone on the relative reinforcing strength of cocaine may be modulated by environmental variables, with greater decreases in cocaine choice observed in monkeys exposed to chronic environmental enrichment versus chronic social stress.
Financial Support: DA10584

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OXYCODONE-INDUCED CONDITIONED PLACE PREFERENCE AND LOCOMOTOR ACTIVITY IN ADULT FEMALE C57BL/6J MICE.

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Aims: Nonmedical use of prescription opioids is a major public health problem in the United States. Furthermore, several studies suggest sex-related differences in prescription opioid responses. As prescription opioid misuse has risen amongst women, it is necessary to better understand the behavioral consequences of oxycodone in females. Previously, we have characterized behavioral effects of oxycodone by the conditioned place preference assay in adult male mice, but we have not investigated oxycodone-induced reward in females.
Methods: We studied 5 groups of adult female C57BL/6J mice (n=7-8) with multiple doses of oxycodone (0, 0.3, 1, 3, and 10 mg/kg; IP) in a conditioned place preference (CPP) paradigm. In the pre-conditioning session, mice were given free access to all chambers for 30 min. During the conditioning sessions, oxycodone or saline injections were paired with black or white conditioning chambers. The post-conditioning session was identical to the preconditioning session. Locomotor activity during conditioning sessions was assessed as number of crosses from one end of the chamber to the other. CPP was calculated as the difference in time spent on the oxycodone-paired side between pre- and post-conditioning sessions.
Results: One-way ANOVA showed a significant preference for the oxycodone-paired side at doses of 1 and 3 mg/kg, $p < 0.05$ and $p < 0.05$, respectively. Two-way ANOVA (Dose x Session) with repeated measures on the 2nd factor showed a dose-dependent increase in locomotor activity ($p < 0.0001$) and increased locomotor activity across conditioning sessions ($p < 0.005$).
Conclusions: In the present study of female mice, we found that oxycodone induced CPP at 1 and 3 mg/kg, but not at 0.3 or 10 mg/kg. Oxycodone produced a dose-dependent increase in locomotor activity and mice showed sensitization to oxycodone's locomotor-activating effects at the doses studied.
Financial Support: This work was supported by NIH 1R01DA029147 (YZ), the Adelson Medical Research Foundation (MJK), and the David Rockefeller Graduate Program (DTC)

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SYNTHETIC CANNABINOID USE IN CANNABIS SMOKERS.

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Aims: Although the passing of the Synthetic Drug Abuse Prevention Act in 2012 classified several chemical classes of cannabinoids as Schedule I substances, the use of synthetic cannabinoids, referred to as 'Spice' (S), is increasing at an alarming rate across the country. The current analysis was performed to assess the prevalence of S use among cannabis smokers volunteering for research studies in New York City.
Methods: Data pertaining to S use were collected over 18 months (2012 –2013) in volunteers responding to advertisements recruiting cannabis-smoking volunteers for studies at NYSPI. Self-reported frequency of use, drug effects, and drug liking were recorded. Use of S by acquaintances were also recorded.
Results: Of the 1351 volunteers, 434 (32%) reporting using S at least once (30 ± 8 years of age; 325 male), 45% used only once, 44% used 2-20 times, 3% used > 20 times, and 5% reported using regularly (weekly / daily). More participants reported disliking the drug relative to those who liked it (65% vs 32%). Compared to cannabis, S was reported to produce a 'different' type of high (34%), shorter in duration (12%), weaker (16%), more intense (13%), or inconsistent (5%). The most frequent effect of S reported was headache (34%); 19% of respondents reported hallucinogenic/ psychotomimetic effects and 11% reported anxiety, panic, and paranoia. A subset reported GI distress (nausea, vomiting; 7%) and 7% reported feeling as if they were "dying" or should go to the hospital; no severe adverse consequences resulting in hospitalization were reported. Among those who never tried S (n = 917, 30 ± 8 years of age; 751 male), 28% reported having friends who smoked S.
Conclusions: The current findings indicate that S is widely used by cannabis smokers and their associates and is an ongoing public health concern. There is an urgent need for controlled studies on the behavioral and physiological risks of synthetic cannabinoids in humans.
Financial Support: NIDA DA09236, DA19239, DA027755

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DIFFERENTIAL INCENTIVE PROCESSING IN YOUTH BEFORE AND AFTER SUBSTANCE USE INITIATION.

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Aims: Adolescence is a period of heightened risk-taking when some youth begin experimenting with drugs and/or alcohol. Understanding the neurobiological response to incentives during adolescence and how it differs in those who initiate substance use is important for identifying youth at the highest risk. Thus, the aim of this study was to characterize incentive processing differences in youth before and after the initiation of substance use.
Methods: Participants were drawn from an ongoing fMRI longitudinal study and scanned on a 3T MRI system. Each participant was scanned at least twice (mean age Time 1: 11.1; Time 2: 15.2). Users initiated substance use between Time 1 and Time 2 (n=7). Controls did not initiate substance use and were matched on age, sex, and family history of alcoholism (n=7). We used a modified monetary incentive delay task to examine hemodynamic responses to anticipated reward and loss. We hypothesized that pre-existing vulnerabilities would present as differences between users and controls at Time 1, and that effects of substance use would present as differences between the two groups at Time 2.
Results: Users showed increased activation in the anterior cingulate for loss anticipation vs. neutral stimuli ($p<.005$, $k>=77$) and no differences for reward anticipation at Time 1. At Time 2, users showed increased activation in the left hippocampus, right thalamus, left insula, and bilateral prefrontal areas for reward anticipation vs. neutral stimuli ($p<.005$, $k>=77$) and no differences for loss anticipation.
Conclusions: These results suggest that pre-use differences in incentive processing exist and may be related to youths' propensity to experiment with drugs and alcohol. Post-use differences may be related to direct and/or indirect effects of substance use. This work is important for understanding who is at the highest risk for initiating drug and alcohol use during childhood and adolescence and potentially developing substance use problems later in life.
Financial Support: Supported by R01 DA027261, R01 AA12217, R37 AA07065, K01 DA020088, and T32 DA7268-22.

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SPECIALIST 'CANNABIS ONLY' CLINICS IN NSW, AUSTRALIA: CLIENT AND TREATMENT CHARACTERISTICS AND ASSOCIATIONS WITH TREATMENT-SEEKING BEHAVIOR.

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Aims: Despite the increase in cannabis treatment seeking there has been no assessment of changes in treatment seeking behaviour for cannabis problems associated with the introduction of these clinics. This study aims to (1) describe the characteristics of clients attending cannabis clinics and compares: (2) treatment seeking history and (3) treatment completion rates between specialist and non-specialist counselling clinics.
Methods: An observational study of administrative information from 209,012 drug and alcohol treatment episodes from services reporting to the NSW Alcohol and Other Drug Treatment Services Minimum Dataset, July 2003 – June 2008.
Results: Across all episodes, cannabis was the second most prevalent primary drug of concern (17.8%, n=37242) after alcohol across all treatment types. The majority of clients seeking treatment for cannabis as a primary concern were male (69.4%, 26088), with a mean age of 29 years. Counselling was the most common cannabis treatment (34.1%, n=12713) with 11.6% (n=1476) of those receiving counselling having done so at a cannabis clinic. Those treated in specialist cannabis clinics were older (30.12 years vs. 27.95 years; $P<0.0001$); had shorter episode durations (10.95 weeks vs. 12.71 weeks; $P<0.0001$); and were more likely to be naïve to treatment (53.7% vs. 47.7%; $p<0.0001$), than those in non-specialist clinics.
Conclusions: Cannabis clinics have attracted groups traditionally difficult to attract and retain in treatment. As the cohort of daily cannabis users age, it is important such dedicated services are attractive to older clients who have not previously sought treatment. Rigorous, prospective research examining client treatment outcomes is now warranted.
Financial Support: The authors are employed by the National Cannabis Prevention and Information Centre, Medicine UNSW which is funded by the Australian Government Department of Health. There is conflict to declare.

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COMPARISON OF THE RISK OF OPIOID OVERDOSE AMONG PATIENTS PRESCRIBED IMMEDIATE-RELEASE AND EXTENDED-RELEASE OPIOID ANALGESICS.

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Aims: This study compared overdose risk among patients prescribed extended-release (ER) versus immediate-release (IR) opioid analgesics. FDA requested revision of labels for ER opioids in response to claims that there is greater risk of overdose and death with ER versus IR opioids. However, little published data evaluates this premise.
Methods: Using a database covering 100 million commercially-insured members between 2008 and March 2012, overdose was assessed by ICD-9 codes for opioid poisoning and overdose (965.00, 965.02, 965.09). Of these, 89% resulted in emergency department or hospital visits. Poisson regression was used to adjust for morphine-equivalent daily dose, age, sedative hypnotic use and psychiatric diagnoses.
Results: Among 9.6 million new opioid users, 92.7% of 585,483 person-years were spent on IR alone, 3.9% on ER alone, and 3.4% on IR and ER opioids concomitantly (IR+ER). There were 3,224 overdoses, of which 44.3% had no opioid prescription within 30 days and 1,796 (55.7%) that did: 1,413 (43.8%) while using IR alone, 70 using ER alone (2.2%), and 313 (9.7%) while using IR+ER. For all opioids combined, overdose risk was 0.26% for IR, 0.31% for ER, and 1.57% for ER+IR per year of use. The adjusted risk ratio comparing overdose risk for ER versus IR opioids was 0.90 (95% CI: 0.70 - 1.15, $p=0.412$), and for IR+ER versus ER opioids was 3.60 (95% CI: 3.05 - 4.26, $p<0.001$). The IR+ER versus IR risk ratio was 2.89 (95% CI: 1.81-4.60) for oxycodone and 6.32 (95% CI: 3.16-12.65) for morphine. Sedative hypnotic use was a strong effect modifier of overdose risk. Patients using IR+ER opioids and sedative hypnotics concomitantly had a 10.6-fold higher adjusted risk of overdose than patients using ER opioids alone (95% CI: 7.29 - 15.47, $p<0.001$), and a 9.9-fold higher adjusted risk than IR opioids alone (95% CI: 8.08 - 12.17, $p<0.001$).
Conclusions: These data indicate that differentiating between IR and ER opioids is not a useful approach to prevent opioid overdose and death, but patterns of opioid use and sedative hypnotic use are.
Financial Support: Purdue Pharma

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96-HOUR METHAMPHETAMINE SELF-ADMINISTRATION IN MALE AND FEMALE RATS: EFFECTS ON BRAIN REWARD PATHWAYS.

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Aims: Recently we have developed a binge and crash model of methamphetamine (MA) self-administration in rats that replicates how human MA users take the drug. Behaviorally this model seems to be relevant to human MA use, but the effects of self-administered binge and crash MA on brain neurochemistry have yet to be characterized. The goal of these experiments was to characterize the effects of this paradigm on the reward pathway in rats. We hypothesized that five weeks of 96-hour MA self-administration will increase dopamine in the reward pathway of female rats when measured immediately following the last self-administration session.
Methods: Male and female (n=4-10/group) rats were implanted with jugular catheters and trained to self-administer MA freely on an FR1 schedule over a period of 96 hours (Monday-Friday) for a total of five weeks. Control rats were paired with MA treated rats in a yoked-saline paradigm. On the fifth week, rats were sacrificed immediately following the last self-administration session on Friday, brain tissue was harvested, collected in punches and analyzed for dopamine, serotonin and norepinephrine via HPLC. Blood was also collected throughout the 96-hour sessions to monitor levels of MA.
Results: Male and female rats demonstrated binge and crash behavior and they also escalated their drug taking over time. Male and female rats did not show any behavioral differences. Female rats showed an increase in nucleus accumbens dopamine compared to saline treated rats. Data were analyzed using a t-test or a two-way ANOVA, where appropriate.
Conclusions: These results suggest that our 96-hour paradigm is both behaviorally and neurochemically relevant to human MA use. This model could lead to more translatable research involving MA abuse and treatment.
Financial Support: No outside funding

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CONTINGENCY MANAGEMENT AND CASE MANAGEMENT FOR OUT-OF-TREATMENT METHAMPHETAMINE USERS.

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Aims: Research has shown that contingency management (CM) has been successful for treatment-seeking methamphetamine (meth) users. However, less studied is the effectiveness of contingency management for out-of-treatment heterosexual meth users.
Methods: This study examined whether CM testing participation and success may associate with changes in drug use over time. Participants were assigned to one of two interventions: contingency management or contingency management plus strengths-based case management (CM/SBCM).
Results: One hundred and seventy participants were recruited through street outreach in Denver Colorado from December 2010 through November 2013. Clients in the CM/SBCM condition attended significantly more contingency management sessions than did clients in the CM condition (8.5 sessions vs. 5.5 sessions; $t = 2.0$, $df = 170$, $p = .047$). CM/SBCM clients also had more clean tests (3.7 vs. 2.6) and, as a consequence, earned more money ($39.00 vs. $28.00), however not significantly. For clients who completed a 6-month follow-up interview ($N = 107$), we examined whether client participation in CM was associated with changes in client drug use – specifically, the reduction of drug use between a client's baseline and follow-up interview. The extent to which participants reduced their drug use was significantly associated with their CM attendance ($p = .001$) and with their money earned in CM ($p < .001$). Multivariate analyses revealed that the effect of CM attendance on drug use was mediated by a client's success during CM sessions. Compared to participants who had never tried to stop using meth, participants who had either tried to stop or had successfully stopped using meth for a period of time attended more CM sessions (10.0 sessions vs. 4.8 sessions; $p < .01$) and earned more money for clean tests ($46.00 vs. $21.00; $p < .01$).
Conclusions: The findings indicate that contingency management both alone and in combination with case management may assist out-of-treatment meth users in reducing drug use.
Financial Support: This study was supported by the National Institute on Drug Abuse, DA026741.

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DO MEDICATIONS IMPACT TREATMENT OUTCOMES? XR-NTX IN COUNTY-FUNDED TREATMENT.

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Aims: The aims were to determine if extended-release naltrexone (XR-NTX) impacts treatment outcomes (engagement, retention, compliance and alcohol use).
Methods: Outcome data collected from the Medication group (XR-NTX) ($n = 190$) were compared to a Post-hoc group of patients ($n = 190$). The Post-Hoc group was matched to the Medication group on primary drug, program type (outpatient or residential), gender, race/ethnicity, age, and fiscal year in treatment. Propensity scores were also calculated using gender, race/ethnicity, primary drug, program types, employment, criminal justice status, mental illness diagnosis, and homelessness at treatment admission.
Outcomes of interest included treatment engagement (stay of at least 30 days), treatment retention (stay of at least 90 days), changes in use, and positive treatment compliance.
Results: Results indicated that the Medication group was more likely when compared to the Post-hoc group to be engaged in treatment (96.3% vs. 72.1%), more likely to be retained in treatment (72.1% vs. 43.7%) and the Medication group was more likely to be discharged from treatment with positive compliance (78.4% vs. 60%). There were no statistically significant differences in primary substance use reported by the Medication group when compared to the Post-hoc group. XR-NTX was also the most significant predictor of engagement ($OR= 12.609$, $p<.001$), retention ($OR= 3.868$, $p<.001$), and positive treatment compliance ($OR=2.766$, $p<.001$).
Conclusions: Due to the voluntary nature of the distribution of the medication, no causal conclusions can be made. However, these results indicate that the use of XR-NTX in conjunction with psychosocial treatment may increase length of stay and treatment compliance. Additional research is needed to determine if these results were due to differences in motivation or other variables not captured in this study.
Financial Support: The Los Angeles County Department of Public Health, Substance Abuse Prevention and Control office supported this research.

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STRATEGIES TO INCREASE FAMILY INFLUENCE ON PATIENT DECISIONS ABOUT MEDICATION-ASSISTED TREATMENT.

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Aims: To accelerate adoption of medication-assisted treatment for opioid and alcohol dependent patients.
Methods: Treatment centers (n=9) and a large commercial health plan formed teams to increase access to medication. Sites received coaching for 3 six-month change cycles. Sites implemented systems changes and adopted, adapted, or abandoned them. Telephone interviews every 7 months captured change strategies, change impacts, and patient engagement with medication-assisted treatment.
Results: Interviews revealed 5 levels of family influence on patient decisions to explore medication options: negative, none, potential, slight, and active. Family education was a key strategy that increased patient engagement with medication-assisted treatment. Sites that made passive efforts to educate family about medications (e.g. allowing family to attend patient education sessions if they showed up) reported fewer prescriptions and/or inductions. Sites that made active efforts built family education into treatment programming (e.g. hosting a Family Day or family seminars with prescribing physicians). Sites with active family engagement reported consistent increases in prescriptions for agonist and antagonist medications. A treatment center reported a 13% increase in the number of patients inducted that participated in their Family Education Program. A second program reported an eight-fold annual increase after adding a family seminar (from 4 per year to 2 per month).
Conclusions: Families do not typically move along the influence continuum without structured, family-targeted programming that supports adoption of medication for alcohol and opioid use disorders. With education, families support patient decisions to use recovery medications. Active family education strategies serve as models for sites with passive family programming.
Financial Support: NIDA Grant R01 DA029716

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ROLE OF NR4A1 (NUR77) AND NR4A3 (NOR-1) IN THE NUCLEUS ACCUMBENS IN CONFERRING THE PROTECTIVE ADDICTION PHENOTYPE FROM ENVIRONMENTAL ENRICHMENT.

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Aims: Environmental enrichment uses social contact, novelty, and exercise to produce a protective addiction phenotype in rats. We are exploring the molecular mechanism of this protection, in particular the orphan receptors NR4A1 and NR4A3. An RNA sequencing experiment found robust changes in both NR4A1 and NR4A3 between isolated and enriched animals that self-administered cocaine or saline. Both transcripts had some of the most robust changes out of nearly 14,000 genes. NR4A1 (Nur77) and NR4A3 (NOR-1) are considered transcription factors and immediate early genes.
Methods: Next generation sequencing and real time PCR from Sprague Dawley rats exposed to cocaine or saline were used to determine induction of NR4A1 and NR4A3. Ongoing studies are examining protein changes of NR4A1 and NR4A3 in environmental enrichment and addiction.
Results: Using RNA sequencing it was found that NR4A1 was more highly expressed in isolated versus enriched rats under basal conditions and was increased by cocaine only in isolated animals. RNA expression of NR4A3 was also decreased by enrichment, but was highly induced by cocaine in both groups. qPCR analysis found NR4A1 in the nucleus accumbens (NAc) peaked at 30 minutes after cocaine with a faster induction with repeated injections. NR4A3 expression in the NAc peaked at 60 minutes and was induced faster and at a higher level with repeated injections.
Conclusions: NR4A1 and NR4A3 are immediate early genes induced by cocaine. These transcripts are also altered by enrichment and may contribute to the environmental enrichment protective addiction phenotype. Ongoing experiments aim at further analysis of this hypothesis.
Financial Support: This work is funded by NIDA grant DA029091.

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A REVIEW OF THE RELATIONSHIP OF DRUG DREAMS WITH CRAVING AND CONSUMPTION.

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Aims: Drug dreams are reported by those actively taking drugs, those in treatment, and those who are abstinent or moderating use after treatment. Researchers and dream theorists have suggested that drug dreams may be directly and indirectly related to craving and consumption, and there is a small but growing body of research investigating these relationships. The current study summarizes the methods and findings of research examining the relationship of drug dreams with craving and consumption.
Methods: Our search of electronic databases and reference lists revealed 28 potentially relevant peer reviewed journal articles and 2 published dissertations. After reviewing the full-text articles, we judged 7 studies to be relevant to our key questions.
Results: Our review indicated three main methods that have been employed to study the relationship of drug dreams with craving or consumption: 1) testing whether "high" cravers experience more drug dreams than "low" cravers; 2) testing the degree to which drug dreams predict subsequent craving, consumption, and drug dreams; and 3) evaluating the relationship of drug dreams with concurrent craving and consumption. Regarding the relationship between drug dreams and craving, 4 studies reported a positive association (i.e., more frequent dreams were related to higher craving) and 1 study reported no association. Regarding the relationship between drug dreams and consumption, 2 studies reported a positive association (i.e., more frequent dreams were related to higher consumption), 2 studies reported no association, and 3 studies reported a negative association (i.e., more frequent dreams were associated with lower consumption).
Conclusions: The implications of these findings will be discussed in relation to several theories regarding the etiology of drug dreams. Although these findings indicate that drug dreams are related to craving and, to a lesser degree, consumption, we recommend further research evaluating the experience of drug dreams in past users who are now abstinent, past users who now engage in moderate use, and current users of various substances.
Financial Support: None

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TEENS' VULNERABILITY TO SUBSTANCE USE DISORDER: EXCESS REWARD OR DEFICIENT INHIBITION?

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Aims: Abused drugs activate dopaminergic (DA) "reward" regions (dorsal and ventral striatum, midbrain), promoting further drug-taking. While adverse effects lead most adolescents to limit risky drug use, some with genetic vulnerabilities to substance use disorders (SUD) and conduct problems, undeterred by risks, press on, developing SUD. We asked: (1) is the enhanced vulnerability of those youths mediated by excess reward-system activity, or by deficient inhibition of risky behaviors; (2) do those mechanisms differ by gender?
Methods: Our fMRI analyses of 41 adolescent patients with severe SUD and conduct problems (20 males) and 40 comparison youths (20 males) continue. In each of 90 risky-decision trials youths decided between pressing a cautious button to earn 1 cent, or a risky one that either won 5 or lost 10 cents. Risky-press "win" odds gradually fell from 0.78 to 0.22. We analyzed brain activity during 4-sec pre-response deliberations with voxel-level and cluster-level FWE correction before risky, and separately before cautious, presses.
Results: Making cautious responses required inhibiting the more-rewarded risky ones; to do so, both male and female comparison youths significantly activated frontopolar, temporal, parietal, or cerebellar regions, or DLPFC, more than patients; the regions differed by gender. No group activated DA regions before cautious responses. Before risky responses all four groups showed reward anticipation, activating DA regions. Comparison boys activated many more, and comparison girls many fewer, DA voxels than patients, but those differences were not statistically significant.
Conclusions: Patients' DA regions did not differ significantly from comparison youths' at the power available here. Before cautious responses comparison youths more than patients activated other regions that may sustain cautious decisions despite temptations (e.g., drug availability, peer pressure). Those control-related regions may underlie patients' and healthy youths' differing vulnerabilities to SUD.
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DRUG-USING ED ASSAULT-INJURED YOUTH: 2-YEAR PROSPECTIVE STUDY OF VIOLENT INJURY AND MORTALITY.

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Aims: This paper describes 2-yr violent injury/mortality outcomes among drug using assault-injured youth presenting to an urban ED
Methods: A prospective cohort study measured 2-yr prevalence of violent injury/mortality among a consecutive sample of youth (14-24) with past 6-month drug use at an urban ED for assault (AI) compared to an age/gender proportionally sampled ED comparison group (CG) of non-assault drug using youth. Youth administered computerized surveys using validated measures at ED visit and at 6, 12, 18, 24 monts. Regression modeling predicted subsequent ED visit for assault over 2 yrs based on medical chart and self-report
Results: 350 AI, and 250 CG youth (82% participation; 53% male, 59% African-American, mean age 20) completed a baseline survey; 85% completed follow-ups. Marijuana was the most common drug used (97%). At baseline, firearm injuries were 20% (n=70) of all injuries in AI group. The AI group had twice the risk for a violent injury requiring ED care over 2 yrs than the CG (36% vs. 22%; OR=2.02). Return visit for firearm injury was higher in the AI group (n=13; 4%) than CG (n=6; 2%). Two-yr mortality was: 1.0% [4 deaths AI (1%), 2 deaths CG (0.8%)]; 5/6 deaths were related to violence (2 firearm) and/or drug use. Regression modeling showed significant baseline predictors of 2-yr ED visit for assault included: female gender (OR=2.3), African American race (OR=2.1), PTSD (OR=3.2), drug abuse/dependence (OR=2.1) and an index visit for assault (OR=2.8). Baseline gun carriage, age, and receipt of public assistance did not predict return visit for assault
Conclusions: Assault-injured youth with drug use have twice the odds of a violent injury within 2 yrs than non-assault drug using youth. Given health disparities in access to services among youth residing in urban areas, interventions at the index visit for assault are urgently needed that address drug use and mental health in order to change future morbidity/mortality for these at risk youth
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DOES NICOTINE DEPENDENCE INDUCE FUNCTIONAL DIFFERENCES IN RESPONSE TO RISK?

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Aims: Drug addiction is characterized by compulsive drug use, despite harmful consequences. It has been hypothesised that an attraction to short term gains despite negative consequences, leads to addiction. Studies investigating regional activation associated with risk-based decision making in drug users have not dissociated probability from magnitude of reward. We used functional magnetic resonance imaging (fMRI) to determine changes in nicotine dependent participants.
Methods: We developed two tasks to investigate aspects of risk; active risk, where subjects choose the magnitude of the gamble, and passive risk, where the risk is dictated to subjects.Nicotine dependent and healthy control subjects (n=15), aged 18-40 years, underwent fMRI whilst completing these tasks. Imaging was performed and echo-planar images were collected using a MR scanner (Siemens 3.0 Trio, Germany).
Results: Response time (RT) and accuracy were analyzed using repeated-measures ANOVAs. Regional activation was identified during the two tasks for high, medium and low risk responses. Data analysis showed significant changes in activation for nicotine dependent subjects compared to controls in medio-frontal regions. There were no significant differences in either RT or accuracy, however the effects of positive or negative outcomes showed differences in future decision making between the two groups.
Conclusions: This study used novel tasks to investigate the effect of nicotine dependence on active and passive risk using fMRI. Clear differences in activation were observed during the evaluation of risk between nicotine dependent and healthy control subjects in medio-frontal regions. Medio-frontal regions alongside the nucleus accumbens are affected by drugs of abuse and are involved in development of drug-dependence, and hence could be the reason we are observing these regional changes.
Financial Support: Australian Research Council
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WEB-BASED SCREENING, BRIEF INTERVENTION, AND REFERRAL TO TREATMENT PROGRAM IN HIGH SCHOOLS.

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Aims: Adolescence is the most critical time to prevent and intervene upon initiated substance use. Apart from developing addiction, adolescent substance use is associated with devastating health and social problems. Screening followed by a brief motivational intervention and when necessary, referral to treatment (SBIRT), can significantly delay onset and reduce use of alcohol and other drugs – but only among those who are not yet addicted. One obvious place to expand SBIRT is in schools. Over the past two years, the Treatment Research Institute (TRI) partnered with Phoenix House (PH) to develop a computerized screening protocol, followed by a tailored Brief Motivational Counseling Intervention delivered by trained substance abuse counselors situated within school-based health clinics. Working with the New York Office of Alcohol and Substance Abuse Services, licensed "health clinics" were created within four New York Metro high schools. Even though the schools and communities were accepting of the program, adolescent SBIRT could not simply be "plugged into" an educational setting without appropriate adaptation and the engagement of state officials, insurers, parents, school staff and community members.
Conclusions: Through this process, we have learned many valuable lessons. Within the framework of an overview of how to develop and implement a successful school-based SBIRT program, we share many of those lessons. This presentation provides the basic foundation for what to consider and how to get started providing SBIRT in schools.
Financial Support: Conrad N. Hilton Foundation

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COGNITIVE BEHAVIORAL THERAPY IMPROVES TREATMENT OUTCOME FOR PRESCRIPTION OPIOID USERS IN PRIMARY-CARE BASED BUPRENORPHINE/ NALOXONE TREATMENT.

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Aims: Aim: To assess whether response to Cognitive Behavioral Therapy (CBT) differed between primarily prescription opioid users (POU) and primarily heroin users (HU) receiving primary care buprenorphine/naloxone (BUP) treatment with physician management (PM).
Methods: Methods: We conducted secondary analyses of a 24-week trial of opioid dependent patients (N=140), categorized as POU (n=49) or HU (n=91), randomized to receive BUP+PM or BUP+PM+CBT. CBT was provided for 45 minutes weekly for the first 12 weeks, with PM only thereafter.
Analysis: Chi-square and t-test comparisons were conducted on baseline variables. Repeated-measures ANOVA was used to evaluate opioid use category (POU vs. HU) by assigned treatment condition on the number of opioid-negative and all drug (cocaine, opioid, benzodiazepine, marijuana, amphetamine) negative urine samples during the two 12-week time periods. Missing weekly urines were considered positive.
Results: Results: Compared to HU patients, POU patients had fewer years of opioid use (p=.06), were more likely to be employed full-time (p=.05), less likely to have had prior drug treatment (p=.002) or detoxification (p=.001), and less likely to report injection drug use (p<.001). Similar percent of HU patients (47%) and POU patients (52%) were assigned to BUP+PM+CBT (p=.59). The mean (SD) number of CBT sessions attended, 7.0 (3.2), and session length 43.2 min (5.2) did not differ by opioid use category (p's>.48). Opioid use category was not significantly associated with response to CBT regarding opioid-negative tests (p's>.17) or treatment retention (p>.61), but moderated the effect of CBT on urines negative for all drugs (p=.03). POU patients assigned to BUP+PM+CBT had over double the mean number of weeks abstinent from all drugs (7.6) compared to those assigned to PM only (3.6; p=.02); HU patients did not differ (5.2 vs. 6.4; p=.70) by treatment condition.
Conclusions: Conclusion: Adding CBT to BUP with PM only improves abstinence from illicit drug use for POU patients.
Financial Support: Supported by NIDA RO1 DA019511

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EFFECTS OF CHRONIC ALCOHOL CONSUMPTION ON COCAINE SELF-ADMINISTRATION IN RHESUS MONKEYS.

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Aims: Although up to 90% of cocaine users also drink alcohol, little is known about how long-term alcohol use interacts with the abuse-related effects of cocaine. In these studies, i.v. cocaine self-administraiton was studied before, during and after monkeys drank ethanol (EtOH) for several months. Mechanisms underlying cocaine/EtOH interactions were assessed using dopamine (DA) receptor antagonists and unconditioned behaviors.
Methods: Eight adult male rhesus monkeys self-administered cocaine (0.01-0.56 mg/kg/injection, i.v.) under a fixed-interval schedule for one hour each morning. Each afternoon (at least three hours later) they were allowed to drink up to 2.0 g/kg of a 4% EtOH/5% Tang solution over one hour. Thus, monkeys were not intoxicated or in withdrawal when self-administering cocaine. Cocaine dose-effect curves were determined before EtOH access and after monkeys had been drinking for ~2 months; doses at which changes in reinforcing effects were observed were determined again starting three weeks after EtOH access was discontinued. The effects of D1- and D2-like receptor antagonists (SCH 23390, eticlopride and buspirone) on self-administration, and the ability of the D3 DA receptor agonist quinpirole to elicit yawning, were conpared when monkeys were and were not drinking EtOH.
Results: Monkeys self-administrered more injections of low cocaine doses during EtOH drinking, an effect that was reversed when EtOH was no longer being consumed. Although EtOH consumption did not systematically alter the effects of DA receptor antagonists on cocaine self-administration, quinpirole-induced yawning was increased.
Conclusions: These results suggest that chronic EtOH drinking leads to increases in the reinforcing effects of cocaine, and implicate D3 DA receptors in these effects.
Financial Support: DA21658

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RACE AS A MODERATOR OF THE RELATIONSHIP BETWEEN DISTRESS TOLERANCE AND CIGARETTE SMOKING AMONG BLACK AND WHITE WOMEN.

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Aims: Black women disproportionately experience smoking-related health consequences despite approximately equivalent smoking rates when compared to White women. Previous research has suggested that cigarette use may represent a stress management strategy for Blacks, but less so for Whites, yet the underlying mechanism of this relationship remains unknown. To that end, the present study examined the role of distress tolerance (DT) and race in relation to smoking.
Methods: 153 women recruited from the community (62.1% White, 37.9% Black) completed a computerized test of DT (PASAT-C) and self-reported lifetime cigarette use. Smoking status was defined with standard criteria as smoking 100 or more cigarettes during one's lifetime and DT was dichotomized according to whether the participant quit (low DT) or did not quit (high DT) the PASAT-C.
Results: To determine the unique predictors of lifetime smoking status, we conducted a logistic regression with two smoking categories, (1) non-smoker and (2) lifetime smoker. In the final model, low DT (OR = 0.23, p =.03), and the interaction between DT and race (OR = 4.58, p = .05) were related to greater odds of being a smoker, such that African American women, but not White women, with low DT were at increased risk for being a lifetime smoker.
Conclusions: While previous literature has suggested that low DT is a general risk factor for cigarette smoking, these findings suggest a unique interaction between race, smoking and DT. These findings add further support to recent work suggesting that negative health behaviors may serve a distress management function for some individuals, and that engagement in certain negative health behaviors may by related, in part, to race.
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NALTREXONE-FACILITATED DISCONTINUATION OF BUPRENORPHINE.

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Aims: Emerging evidence suggests that rebound kappa receptor agonism may be implicated in some of the discomfort associated with discontinuing buprenorphine. The purpose of this investigation is to assess the tolerability and feasibility of using naltrexone, a mu and kappa antagonist, to facilitate buprenorphine discontinuation in stable individuals previously unable to discontinue.
Methods: Individuals maintained on 2 mg or less of buprenorphine, with previous discontinuation failures, and with a clinically appropriate reason for discontinuation were admitted into this 6-week protocol. Buprenorphine discontinuation and naltrexone induction were carried out during an 8-day inpatient stay. Starting on day 4, participants were provided four daily escalating doses of PO naltrexone (6.25, 12.5, 25mg, and 50 mg), followed by IM depot on day 8 (380 mg). SOWS and other measures were administered daily. Individuals were followed weekly for five weeks after discharge, and follow-up occurred at 3 months and 6 months.
Results: 5 individuals (mean buprenorphine dose 1.2 mg) have completed the protocol thus far. No participants experienced an increase in withdrawal symptoms during induction onto naltrexone (day 4 and onwards). Further, by day 8, mean SOWS scores had dropped significantly below those obtained just prior to initiating PO naltrexone (22.7 + 7.9. before vs. 5.2 + 2.7 after by paired t test, $p<0.05$). There were no serious or unexpected adverse events. All participants remained free of opioids, including buprenorphine, at each weekly visit by urine toxicology, and remained opioid-abstinent at 3 and 6 months by self-report.
Conclusions: These preliminary findings suggest that naltrexone-facilitated buprenorphine discontinuation represents a feasible strategy for individuals who otherwise have difficulty tolerating discontinuation. Future studies can investigate the efficacy of this approach, as well as the feasibility of an outpatient protocol.
Financial Support: This project was supported by the following NIDA grants: DA022412, DA031771,
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SEX DIFFERENCES IN FOSB EXPRESSION IN REWARD CIRCUITRY AFTER ADMINISTRATION OF COCAINE, METHAMPHETAMINE, AND CANNABINOIDS.

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Aims: Both preclinical and clinical studies have shown sexually dimorphic patterns in behavioral responses to cocaine in all phases of the cocaine addiction process (induction, maintenance, and relapse). Thus, a clear picture is emerging which suggests that the biological basis of sex-specific differences in cocaine addiction resides in the disparate regulation of the CNS between sexes. New evidence now shows that cocaine-induced alterations in the PKA intracellular signaling is also sexually dimorphic and that the estrous cycle differentially affects it. It is yet to be determined if, similar to cocaine, the sexual dimorphic intracellular responses are seen after depressant and/or other type of stimulant drugs. The aim of this study was to determine if there are differences between male and female expression of FosB in reward associated areas after administration of cocaine, methamphetamine (METH), or WIN-55.
Methods: Both female and male rats were injected with cocaine (30 mg/kg), METH (3 mg/kg), WIN (an agoinst of cannabinoid receptors; 0.15 mg/kg), saline (1 cc) or DMSO (1 cc).
Results: Female rats in the cocaine group showed higher levels of FosB expression in the nucleus accumbens (NAc) and the prefrontal cortex (PfC) when compared to control. However, in the PfC, sex differences in the pattern of Fos B expression were seen after cocaine administration. In male rats, WIN treatment significantly increased FosB expression in the NaC and PfC when compared to control.Furthermore, male rats also displayed a higher expression of FosB than did females.
Conclusions: Taken together, our results suggest a sexually dimorphic response of FosB in reward associated areas after all three treatement, which could account for previously reported behavioral differences to stimulants.
Financial Support: NIH/NIDA R24-012136, RCMI RR03037, and NIH MBRS/RISE GM060665

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WHEN LESS IS MORE: A WEB-BASED STUDY OF USER BELIEFS ABOUT BUPRENORPHINE DOSING IN SELF-TREATMENT OF OPIOID WITHDRAWAL SYMPTOMS.

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Aims: There is growing evidence of an alarming increase in the illicit use of buprenorphine in the U.S., but our understanding of its use remains limited. This study aims to explore Web-based data on illicit buprenorphine use, focusing on user beliefs about the appropriate dosing in self-treatment of opioid withdrawal.
Methods: A web forum that allows free discussion of illicit drugs and is accessible for public viewing was selected for analysis. Posts that contained discussions of buprenorphine and opioid withdrawal symptoms were retrieved using PREDOSE, a novel semantic web platform developed for the information extraction and analysis of social web data on illicit drugs. All unique user names were anonymized. A total of 1,140 posts were retrieved, covering a time period between 2005 and May, 2013. These posts were uploaded to an NVivo database. A random sample of 378 (33%) posts was selected for content analysis.
Results: The number of buprenorphine-related posts increased from 46 in 2005 to 1,012 in 2009 and 4,376 in 2011. Over 65% of coded posts that contained information about buprenorphine dose in the self-treatment of withdrawal symptoms, endorsed and/or advocated, use of significantly lower amounts of buprenorphine (2 mg and lower) than typical doses of 16-24 mg per day recommended for standard treatment. Such posts expressed a belief that lower doses of buprenorphine are more effective in the self-treatment of opioid dependence, while the physician-prescribed dosage is too high. Thus, prescribed doses can be "conserved" or shared with others.
Conclusions: Social web data suggest that the "less is more" approach to buprenorphine dosing may be fairly prevalent among illicit opioid users and may be one of the contributing factors to the increasing availability of diverted buprenorphine. Our findings highlight the importance of Web-based data in drug abuse epidemiology research.
Financial Support: Financial support was provided by NIDA (R21DA030571; Daniulaityte, PI; Sheth, PI)

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BUPRENORPHINE/NALOXONE ABUSE AND DIVERSION: FILM RATES ARE LESS THAN TABLET RATES.

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Aims: Previous reports showed differences in diversion and abuse rates between buprenorphine formulations, but observation periods were short. This study extends the comparison of diversion and abuse rates between buprenorphine sublingual formulations.
Methods: Data from the Researched Abuse, Diversion, and Addiction-Related Surveillance (RADARS®) System Drug Diversion (DD), Opioid Treatment (OTP), and Survey of Key Informants' Patients (SKIP) Programs were analyzed. The DD program captures new police investigations. The treatment programs (OTP and SKIP) collect patient reports of using a product "to get high" in the previous 30 days. Quarterly data from 2010Q4-2013Q1 (DD) and 2011Q2-2013Q1 (OTP/SKIP) were analyzed. Event ratios (rates) were based on the number of patients filling prescriptions for each formulation ("Unique Recipients of a Dispensed Drug," URDD). Average rates and 95% confidence intervals (CIs) were calculated using negative binomial regression.
Results: 1,505 diversion reports and 5,293 abuse reports were analyzed.
Average diversion rates for buprenorphine/naloxone tablets (13.6 reports/10,000 URDD; 95% CI: 12.8-14.5) and monoingredient tablets (8.7; CI: 7.6-9.8) exceeded the combination film rate (1.3; CI: 1.1-1.5) (Rate ratio (RR) c/w film: 10.6 (CI: 9.0-12.4; p<0.0001) for combination tablets and 6.7 (CI: 5.5-8.2; p<0.0001) for monoingredient tablets).
Average abuse rates for buprenorphine monoingredient tablets (61.8 reports/10,000 URDD; CI: 59.2-64.6) and buprenorphine/naloxone tablets (21.3; CI: 20.3-22.3) exceeded the combination film rate (9.1; CI: 8.7-9.6) (RR c/w film: 6.8 (CI: 6.3-7.3; p<0.0001) for monoingredient tablets and 2.3 (CI: 2.2-2.5; p<0.0001) for combination tablets).
Conclusions: Diversion and abuse rates for buprenorphine and buprenorphine/naloxone tablets consistently exceed those of buprenorphine/naloxone sublingual film.
Financial Support: Reckitt-Benckiser Pharmaceuticals

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MARIJUANA USE, MOTIVES, AND CHANGE INTENTIONS IN ADOLESCENTS.

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Aims: While marijuana (MJ) users report various motives for use, a majority of adolescent marijuana users express a desire to reduce MJ use or abstain. This study aimed to examine the relations between motives to use and abstain from MJ, past use and attempts to reduce or quit use, intention to use, probability of quitting, and intention and desire to cut down or stop using.
Methods: 162 adolescent MJ users completed a school-based online survey.
Results: MJ motives were associated with lifetime and past 30 day use. Intention to use was primarily influenced by use motives, specifically enhancement (B = .33, SE = .10, p < .001), expansion (B = .32, SE = .11, p < .01), and conformity (B = -.36, SE = .15, p < .05) motives, although negative consequences motives to abstain (B = -.31, SE = .16, p < .05) were inversely related. Low social motives to use were associated with intention (B = -.28, SE = .15, p < .05) and probability (B = -.31, SE = .14, p < .05) cessation variables, suggesting that using MJ for social facilitation may be a barrier to quitting. High personal/peer beliefs motives to abstain also predicted probability of quitting (B = .41, SE = .17, p < .05) and desire to quit (B = .58, SE = .15, p < .001), further demonstrating the influence of social factors. Negative consequences motives to abstain were also associated with intention to quit (B = .41, SE = .17, p < .05), showing that this particular motive may be more likely to facilitate the actualization of quitting behavior.
Conclusions: The relation of use motives to use behavior was consistent with past research. Use motives dominated models for intended use, whereas both motives to use and abstain influenced quitting variables. Motives seemingly differentially affect particular aspects of cessation and may be helpful in developing motivation-based substance prevention and intervention programs that aid in predicting continued use, cessation, and susceptibility to relapse.
Financial Support: R01AA012171-11A1 - Facilitating Adolescent Self-Change for Alcohol Problems

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RISK-TAKING BEHAVIOR OVER 36-MONTH FOLLOW-UP TREATMENT IN OUTPATIENT OPIOID MAINTENANCE TREATMENT PROGRAM.

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Aims: To assess the change in Risk-taking behaviors among opioid use disorder patients in treatment in outpatient addiction clinics in Aquitaine, France between 1994 and 2012.
Methods: Opioid use disorder patients were assessed at treatment entry and every 6-month thereafter for 36 months with the Addiction Severity Index (ASI), the Risk Assessment Battery (RAB) and blood tests for HIV and HCV sero-status. We assessed the changes of risk-taking behavior over these four periods (MANOVA). Multivariate analyses were performed to define the factors associated with risk-taking behaviors.
Results: 883 patients were included (74% males, 32.4 y.o.). There was a significant decrease of the number of patients who reported drug-related risk-taking behavior (from 36% to 15%) over the 36-month follow-up. This decrease occurred within the first 6 months then remained stable, but there was a significant decrease in the severity. There was a significant decrease of the number of patients who reported sex-related risk-taking behavior (from 44% to 39%). This decrease occurred within the first 6 months then remained stable, but there was a significant decrease in the severity. Patients who reported Drug-related risk-taking behavior were more likely younger (< 32 y.o.), HCV+, still opiate users, heavy alcohol users (more than 5 AU per day), and presented current psychiatric disorder. Patients who reported Sex-related risk-taking behavior were more likely female, HIV-negative, still opiate users, alcohol users, and presented current psychiatric disorder. There was no association with previous treatment, year of opiate use, severity of addiction at baseline, neither year of treatment entry.
Conclusions: Risk-taking behavior decreased within treatment. Factors associated with risk-taking behaviors were similar at baseline and throughout the follow-up period. Additional prevention strategies might be needed for younger patients, female and those with psychiatric comorbidity.
Financial Support: PHRC 1994, PHRC 2000, PHRC 2006, MILDT/INSERM 2004

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PSYCHOMETRIC EVALUATION OF THE MARIJUANA REDUCTION STRATEGY SELF-EFFICACY SCALE WITH A COMMUNITY SAMPLE OF MARIJUANA USERS.

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Aims: We designed this study to evaluate the cue reactivity, reliability, and validity of a questionnaire assessing community marijuana users' self-efficacy to employ, and recent past use of, 21 specific cognitive-behavioral strategies to reduce their use of marijuana.
Methods: Using a web-based recruitment and data-collection procedure, 513 regular marijuana users from North America, Europe, and Australia/New Zealand completed our measure following exposure to an audiovisual presentation of either marijuana stimuli or control stimuli, followed by completion of other measures of their marijuana use.
Results: Reliability analyses in the current sample supported interpreting all 21 strategies as comprising a single scale. Although cue exposure led to a significant increase in craving between conditions, there was no significant difference in scores on the reduction strategy self-efficacy scale. Reduction strategy self-efficacy scores were significantly positively correlated with self-efficacy to abstain from marijuana and with recent past use of these strategies. Additionally, self-efficacy was significantly negatively associated with quantity and frequency of marijuana use and with marijuana-related problems; however, use-reduction self-efficacy was only weakly correlated with general self-efficacy. The most frequently reported reduction strategies reflected using marijuana only once per day, turning down unwanted hits, and not keeping a large stash available or not obtaining more marijuana right away if one's supply runs out.
Conclusions: Taken together, these findings support the psychometric properties of the questionnaire in a large community sample of regular marijuana users. The questionnaire should be widely applicable in clinical and research settings because it is easily readable, can be completed in a matter of minutes, and is unlikely to burden most people. In addition, rating one's confidence to employ each strategy listed on the scale might serve as a form of education by informing users of strategies of which they are otherwise unaware.
Financial Support: None

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EFFECTS OF FAMILY RELATIONSHIPS QUALITY ON DRUG USE: MEDIATING EFFECTS OF MORAL CONVICTION.

Alexandra N Davis, Gustavo Carlo, Cara Streit; University of Missouri, Columbia, MO

Aims: Aims: Previous research demonstrates the importance of both family relationships and moral development in predicting substance use. The present study will extend this literature by examining the mediating role of moral conviction (i.e., strength of moral motivation) in the associations between parent and sibling relationship positivity and substance use outcomes (i.e., tobacco use, alcohol use, binge drinking, and marijuana use). We hypothesized that family positivity would be positively associated with moral conviction, and that moral conviction would be negatively associated with substance use.
Methods: Method: Participants were 303 college students (M age = 18.71; 62.7% female). Participants completed measures of mother, father, and sibling positivity, their moral convictions regarding substance use, and their frequency of tobacco, alcohol, marijuana, and binge drinking in the past year.
Results: Results: Structural path analysis was conducted to examine the relations among the study variables. The model displayed acceptable fit ($\chi 2$=2.74; CFI=.98; RMSEA=.08). The results demonstrated that sibling positivity was positively associated with moral conviction, which in turn, was negatively associated with the substance use. Parental positivity was also directly associated with substance use. These results provide support for partial mediation of moral conviction in the associations between relationship quality and substance use. Future analyses will examine potential gender differences.
Conclusions: Conclusions: The findings address important gaps in the literature by demonstrating the importance of both parent and sibling relationship quality on substance use, as well as examining the strength of adolescents' convictions in accounting for college students' substance use. The discussion will focus on the influence of both family relationship quality and moral convictions in predicting substance use outcomes.
Financial Support: Financial Support: Mizzou Advantage Grant from the University of Missouri.

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CRACK COCAINE USE AND PERCEIVED LIFE CHANCES.

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Aims: Adolescents who perceive limited potential future success are at risk for substance use. This study investigates the utility of the Perceived Life Chances scale (PLCS) to model crack cocaine use with an adult (Mage = 35.7 years, SD = 14.51 years) street population (N=332) specifically, the association between the PLCS and whether participants have: ever used crack, age of first use of crack, and number of days used crack.
Methods: In addition to the PLCS, the participants were administered the Risk Behavior Assessment.
Results: The PLCS was negatively related to the decision to use or not use crack cocaine. In contrast to our hypotheses, greater pessimism was related to an older age of first use and not associated at all with the number of days using crack cocaine. The strong covariates of crack cocaine use included: sex trading for either drugs or money; use of other drugs such as opiates, powder cocaine, and marijuana; and history of sexually transmitted infections such as gonorrhea, syphilis, and Chlamydia.
Conclusions: PLC has implications for the use of Decisional Balance in interventions with crack users in that those who predict a bleak future for themselves may only value immediate consequences of their drug use behavior and may not value long-term negative consequences given that they are pessimistic about their long-term opportunities.
Financial Support: The project described was supported by Award Numbers R01DA030234 from the National Institute on Drug Abuse, P20MD003942 from the National Institute of Minority Health and Health Disparities, and ID10-CSULB-008 from the California HIV Research Program.

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PRENATAL CIGARETTE SMOKE EXPOSURE, CHILDHOOD AGGRESSION AND ADOLESCENT CIGARETTE USE.

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Aims: Studies have demonstrated a relation between prenatal cigarette smoke exposure (PCSE) and subsequent smoking among exposed offspring. There is also a relation between PCSE and child behavior problems. In this prospective study of teenage mothers, we examined a potential pathway to adolescent smoking in offspring via childhood aggressive behavior.
Methods: Pregnant teenagers (n = 413) were recruited from an urban prenatal clinic and interviewed during pregnancy. Mothers and children were assessed at delivery and during follow-up visits when the children were 6, 10, 14, and 16 years old. The PCSE measure was maternal report of any cigarette use during the third trimester. Our outcome measure was self-reported current smoking in offspring at the age 16 follow-up. Child aggressive behavior was measured with the Child Behavior Checklist (CBCL) at age 6. Path analysis using Mplus evaluated proposed pathways and tested for an indirect effect of PCSE on adolescent cigarette use through childhood aggressive behavior.
Results: Half of the offspring in this cohort had PCSE, and PCSE significantly predicted child aggression at age 6 (p=.011, one-tailed). By the age 16 follow-up visit, 20% of the adolescents were smokers (14% of the non-exposed and 22% of the exposed offspring). Adolescent cigarette use was directly associated with age 6 aggression scores, less strict parenting during adolescence, and White race. There was also an indirect path between PCSE and adolescent cigarette use via age 6 aggression scores (p=.035, one-tailed).
Conclusions: We found that childhood aggression was a significant pathway linking PCSE to adolescent cigarette use. These results suggest several opportunities for early intervention with mothers who smoke and exposed offspring. A two-pronged approach addressing both maternal and child behavior may help prevent cigarette use in the next generation. Future work should examine potential mediators and moderators including maternal stress, maternal aggression and child association with deviant peers.
Financial Support: AA08284; DA009275; DA025734

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THE IMPACT OF OPIOID SUBSTITUTION THERAPY ON MORTALITY POST-RELEASE FROM PRISON.

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Aims: Mortality following release from prison is high-risk for mortality. We examined the impact of opioid substitution therapy (OST) for opioid dependence during and after incarceration, upon mortality post-release.
Methods: A cohort included all opioid dependent people who entered OST in New South Wales, Australia, 1985-2010, released from prison at least once, 2000-12 (N=16,453). We linked data on OST history, court appearances, prison episodes, and deaths. N=60,161 eligible prison releases occurred. Demographics, criminographic and treatment histories were examined; crude mortality rates (CMRs) calculated according to retention in OST; and Cox regressions run to examine the association between OST exposure (a time dependent variable) and mortality in the post-release period.
Results: Individuals were observed for 100,978 person-years post-release; 1,050 deaths occurred. Most received OST sometime while incarcerated (76.5%); individuals were receiving OST in 40% of releases. Lowest post-release mortality was among those continuously retained in OST post-release, highest among those with no OST. Multivariable models showed OST exposure in the 4 weeks post-release reduced hazard of death by 75% (adjusted hazard ratio 0.25; 95%CI: 0.15, 0.52); OST receipt in prison had a short-term protective effect that decayed quickly across time.
Conclusions: OST in prison and post-release reduces mortality risk in the immediate post-release period. OST in prison should be scaled up, and post-release OST maximised.
Financial Support: Australian National Health and Medical Research Council; Australian Institute of Criminology (AIC); Australian Government Department of Health and Ageing.

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FLORIDA'S PRESCRIPTION DRUG MONITORING PROGRAM AND OXYCODONE-CAUSED MORTALITY: A MONTHLY TIME SERIES ANALYSIS, 2003-2012.

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Aims: In Florida, oxycodone-caused deaths declined substantially (52%) from peak levels of 126 (2010) to 61 per month (2012). Several important pharmacy, law enforcement, and health policy factors likely contributed to this decline, including the implementation of Florida's prescription drug monitoring program (PDMP). In the current study, we examine whether the PDMP had an effect on oxycodone-caused mortality.
Methods: We used a time-series, quasi-experimental research design, including internal (Florida) and external (New York City) controls for comparison. The dataset included 120 monthly observations of oxycodone-caused mortality in Florida over a 10-year period (2003–2012). We used an autoregressive integrated moving average (ARIMA) model with covariates. We operationalized the introduction of re-formulated Oxycontin® (pharmacy), Operation Pill Nation (law enforcement), and Florida House Bill 7095 (health policy) using a single continuous variable representing the number of pain clinics closed in Florida.
Results: Oxycodone-caused mortality declined by 4.1% [CI: 0.97%,7.25%] after the implementation of Florida's PDMP in October 2011, or approximately 30 deaths averted annually. The association remained after excluding decedents with alprazolam. However, mortality from all opioids exclusive of oxycodone did not change
Conclusions: This is the first study to show that the PDMP had a significant impact on
reducing oxycodone-caused mortality in Florida. These results have implications for national efforts to reduce the negative outcomes related to the prescription drug epidemic.
Financial Support: University of Florida

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RECENT CANNABIS USE AMONG ADOLESCENT AND YOUNG ADULT IMMIGRANTS IN THE NETHERLANDS: THE ROLES OF ACCULTURATION STRATEGY AND LINGUISTIC ACCULTURATION.

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Aims: The cultural values paradigm proposes that cultural values of the host country shape attitudes and behaviors toward substance use, thereby promoting or protecting against substance use. Following this theory, becoming more acculturated to a culture with more positive values toward substance use will increase the risk of substance use. This study examined the relation of linguistic acculturation and the acculturation strategies integration, separation and marginalization with past year cannabis use among immigrant adolescents and young adults. Additionally, we studied the mediating role of affiliation with cannabis-using peers.
Methods: Data were utilized from i4culture, a Dutch study on immigrants aged 15-24 years. Participants belonged to the five largest immigrant populations in the Netherlands. In total, 771 adolescents and young adults (mean age 19.29, SD=2.61, 53.8% female) from Surinamese (n=210, 27.2%), Moroccan (n=209, 27.1%), Turkish (n=110, 14.3%), Antillean (n=109, 14.1%), and Asian (n=133, 17.3%) backgrounds participated. With questionnaires, past year cannabis use, acculturation strategy, linguistic acculturation, and affiliation with cannabis-using peers were assessed.
Results: Using logistic regression analyses, we found no relation between acculturation strategy and past year cannabis use (OR=1.25, p= .38 for separation vs integration and OR=0.86, p= .50 for marginalization vs integration). Linguistic acculturation was positively related to cannabis use (OR=2.20, p< .01). Affiliation with cannabis-using peers partly mediated this relation (OR=1.09, p< .01).
Conclusions: Non-Western immigrant youngsters who speak the host culture's language at home are more likely to use cannabis than youngsters who speak their native language at home. The former group is more likely to affiliate with cannabis-using peers, which partly explains their increased risk of cannabis use.
Financial Support: ZonMW, the Netherlands, 60-60600-97-154

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INDIGENOUS CULTURE AS INTERVENTION IN ADDICTIONS TREATMENT.

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Aims: Drug addiction among Indigenous peoples is a health concern in Canada. The aim of our community-based team's work is to evaluate the effectiveness of First Nations culture as a health intervention in alcohol and drug treatment. Phase I developed a wellness framework and identified cultural interventions based on our research findings.
Hypothesis: Health for First Nations is broadly envisioned as wellness and is understood to exist where there is physical, emotional, mental, and spiritual harmony.
Methods: We gathered understanding of how Indigenous traditional culture is understood and practiced at a sample of 12 First Nations residential treatment programs by undertaking a three day environmental scan led by an Indigenous Elder; this constituted Phase I of our study.
Results: Our work resulted in the development of a wellness framework addressing physical, emotional, mental, and spiritual wellbeing and the identification of 22 cultural interventions to facilitate wellness. These results were verified among our team members, participating treatment centres and their communities at large.
Analysis: We prioritized Indigenous knowledge in our data analysis. In doing so, we applied 3 'lenses' or approaches to analyzing the information we collected across the treatment centres. We involved: (1) treatment centre environmental scan participants (staff, clients and community members), (2) Indigenous knowledge keepers (Elders), and (3) our Western-trained research team members.
Conclusions: Indigenous knowledge shares that traditional culture is vital for client healing. However, there is a serious absence of empirical documentation of its impact on client wellness. Our project is the first of its kind in Canada and is suitably timed with renewal processes underway in Canada's First Nations addictions treatment system. A key recommendation of the renewal has been the establishment of a culturally competent evidence base to document the nature and demonstrate the effectiveness of cultural interventions within treatment programs.
Financial Support: Canadian institutes of health research

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IMPACT OF 20 YEARS HARM REDUCTION POLICY ON HIV AND HCV AMONG OPIOID USERS NOT IN TREATMENT.

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Aims: To assess the change in sero-status for HIV and HCV and Risk-taking behaviors among opioid users not in treatment in Aquitaine, France between 1994 and 2012, knowing that major changes in French Public Health Policy occurred during this period.
Methods: Opioid use disorder individuals were assessed before treatment with the Addiction Severity Index (ASI), the Risk Assessment Battery (RAB) and blood test for HIV and HCV sero-status. Four periods corresponding to changes in French Public Health policy were defined (1994-1995, 1996-1999, 2000-2005, 2006-2012). We assessed the changes of HIV, HCV, and risk-taking behavior over these four periods (ANOVA, Cochran-Armitage). Multivariate analyses were performed to assess the link between time period and change in these variables.
Results: 883 individuals were included (74% males, 32.4 y.o.). There was a significant decrease in mean years of opioid use (10.3 years to 5.8) (F(3,867)= 24.6, p< .0001). The IV route was predominant from 1994 to 2005 and decreased thereafter, while nasal route became the main route. The other routes (smoking, oral) increased also but reported by 10% or less. The prevalence of HIV-positive decreased since 1996 among the whole sample (Z= 9.2, p< .0001) and also among the IV users only (Z= 6.2, p< .0001). The prevalence of HCV- positive decreased significantly since 2000 among the whole sample (Z= 11.7, p< .0001), but only since 2006 among the IV users only (Z= 4.9, p< .0001). Among IV users past 6 months (n= 467, 53%), those enrolled after 1995 were less likely to share injection material and paraphernalia. Among individuals reporting sexual intercourse past 6 months (n= 608, 69%), those enrolled in 2006 and thereafter were more likely to report systematic condom use.
Conclusions: Results confirmed the impact of harm reduction policy on HIV prevalence and showed a reduction on HCV prevalence on opioid users. Further studies are needed to confirm this reduction in out-of-treatment drug users not seeking treatment and other drug users (e.g. cocaine, crack).
Financial Support: PHRC 1994, PHRC 2000, PHRC 2006, MILDT/ INSERM 2004

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OPIOID USE DISORDERS: TRENDS AND CORRELATES.

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Aims: The aims of this poster are to 1) explore the trends in opioid use disorders overall, by age and geography and 2) examine differences in the liability for addiction based on age of onset.
Methods: Methods: Data are from the 2011 National Survey on Drug Use and Heath (NSDUH), 2011 Drug Abuse Warning Network (DAWN), and 2011 Treatment Episode Data Set (TEDS).
Results: From 2002 to 2011 the number of people with opioid use disorders rose 38%. The number of people with prescription opioid use disorders is 3 times higher than heroin use disorders, but the increase of heroin use disorders was higher (104%). Over half the people with prescription opioid use disorders were over the age of 25, but the rate of growth was highest (+55%) among those age 18-25. From 2004 to 2010, this has been a 42% rise in drug related emergency room admissions, with the rates particularly high for prescription opioid alone (132%), prescription opioid + other illicit drugs (139%), prescription opioid + alcohol (+63%) or prescription opioid + illicit drugs + Alcohol (+94%). From 2000 to 2010, there has been a 44% increase in opioid related treatment admissions overall, including 352% for prescription opioids. The rate of growth of prescription Opioid Treatment admissions are growing even more rapidly for young adults ages 18 to 24 (+489%).
Conclusions: The rapid growth in opioid use disorders is being driven by prescription opioid use disorders. While most people are adults, the rate of growth among young adults is much faster and also raises the potential for years of problems ahead. Geographic variation in the rates of disorders suggest that availability and local practices are significant, and that it may be feasible to stop the further rates of disorder or even reverse it. The return of opioids also has important implications for the need to have detoxification and medication assisted treatment services available as part of health care reform.
Financial Support: NIDA Grant no. R37 DA011323

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ECOLOGICAL MOMENTARY ASSESSMENT TO PREDICT THE RISK OF RELAPSE.

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Aims: To demonstrate the feasibility and accuracy of EMA collected by smartphone to predict the risk of relapse within the next 7 days.
Methods: Data were collected from 52 clients post treatment who where 48% Female, 65% Black, 4%Hispanic, 56% adolescent, 4% weekly alcohol users, & 23% weekly other drug users. Participants received a smartphone and data plan for 6 weeks. They completed 90% of 6 EMA/day at 6 random times (4860 total observations). Each 2 minute EMA was about the past 30 minutes and asked who the participant was with, where they were, what else they were doing, and what they were feeling. Participants were asked to rate the extent which area made them want to use alcohol/drugs, or supported their recovery. They were also asked whether they were using and to rate other factors related to relapse including withdrawal, craving, physical pain, ability to resist using, and exposure to drugs and alcohol. The combined ratings (alpha=.93) were used to predict the risk of subsequent alcohol or drug use based on self-report in the next 42 EMA or weekly urine tests. CHAID was used to check individual items that could improve the prediction model.
Results: The analysis identify 5 main risk groups: 1) Current use or withdrawal (381, 14% of observation), 2) High risk (145, 5%), 3) Moderate risk (836, 31%), 4) Low Risk (560, 20%) and 5) Denial (804, 30%). Relative to the low risk group (8% subsequent use OR=1.0), the moderate risk (26%, OR=3.9) and high risk (66%, OR=20.5) were significantly more likely to use in the next 7 days. Regardless of their scale score, those who had used or experienced withdrawal symptoms in the past 30 minutes were even more likely to use in the next week (95%, OR=32.3). The denial group, who perceived literally no risks and complete support, where actually at moderate risk of relapse (35%, OR=5.8).
Conclusions: The feasibility and effectiveness of using smart phones to monitor and predict the risk of relapse in the near future creates an opportunity to intervene prior to use and improve the effectiveness of recovery management.
Financial Support: NIDA DA011323, DA021174

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SUBSTANCE USE TRAJECTORIES FROM EARLY ADOLESCENCE THROUGH THE COLLEGE YEARS.

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Aims: The transition from adolescence into adulthood is an important period for the development of alcohol, marijuana, and hard drug use. Prior research has explored patterns of substance use in adolescents to assist in understanding how use develops (Schulenberg & Maggs, 2008). However, little is known about changes in patterns across high school and college, and whether individual factors affect these changes. The aims of this study were to identify distinct patterns of substance use and to explore the impulsive trait correlates of these trajectories.
Methods: Participants were 451 college freshmen (48% male). At the first assessment, participants reported on substance use from age 13 until present, and completed a measure of multifaceted impulsivity, the UPPS (Whiteside & Lynam, 2001). Participants were then followed longitudinally for two additional years to assess substance use.
Results: Group-based trajectory modeling, performed using the PROC TRAJ application, was used to estimate developmental trajectory groups. Trajectories were estimated using ten data points per individual representing average weekly use for each year from age 13 to 22. Visual inspection of the trajectories indicated increases in substance use immediately upon college entry. Results supported a five-group model of alcohol use, a four-group model of marijuana use, and a two-group model of hard drug use. Across all substances, the probability of escalating in trajectory class was characterized by sensation seeking, whereas continued heavy alcohol and hard drug use into adulthood are characterized by impulsivity under the condition of negative emotions.
Conclusions: These results suggest confirm that the start of college is an important developmental transition in terms of poly-substance use. In addition, although the trait of sensation seeking appears to relate to trends in the early stages of use, other traits of impulsivity become relevant when determining which individuals go on to chronic, problematic use.
Financial Support: This research was supported by grants from the National Institute on Drug Abuse (DA005312 and DA007304).

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HIV AMONG PUERTO RICAN PEOPLE WHO INJECT DRUGS: HEALTH DISPARITIES CONTINUE.

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Aims: To describe health disparities related to HIV among Puerto Rican people who inject drugs (PRPWID) in the Northeast US (NE) and Puerto Rico (PR), and provide recommendations to address them.
Methods: Background: Higher HIV risk behaviors, prevalence, incidence and mortality among PRPWID have been reported in the NE and PR since early in the epidemic. Now that advances in HIV prevention and care have raised the possibility of an AIDS-free generation in the US, an examination of HIV prevention and care for PRPWID in these regions is needed.
Results: Sustained Disparities: In 2010, drug injection accounted for about 9% of incident HIV infections in the US, 16% in the NE and 20% in PR. Data from the NE and PR continue to show that Hispanics (primarily Puerto Rican) are more likely to have HIV attributed to injection drug use. In NYC Hispanics represent over 50% of all IDUs, and 45% of PWID who are newly infected (over one-third born in Puerto Rico). Numerous studies have documented the lower availability of HIV prevention tools (e.g., NEPs) in PR, as compared with the NE, and the narrower range of drug treatment services. ART provision in PR has been inconsistent, and higher mortality rates among PLWH in NY is reported among those born in Puerto Rico. Importantly, related comorbidities among PWID, including overdose deaths and Hepatitis C, also have high prevalence among PRPWID.
Conclusions: PRPWID continue to be over-represented in the HIV/AIDS epidemic, and have not received maximum benefit from advances in prevention and treatment. Despite recent efforts to expand services in PR, more severe disparities are found there than in the NE. While the "airbridge" from PR to the mainland enables PRPWID to access services, inadequate service provision in PR influences the success of prevention/care efforts in the NE, for HIV and other comorbidities of PWID. To address these disparities and reach the goals of the national HIV/AIDS strategy, innovative collaborative approaches that span geographic areas are needed.
Financial Support: Financial Support: NIDA Grant P30DA011041

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RISK OF POLYSUBSTANCE USE AND CO-OCCURRING INTERNALIZING AND EXTERNALIZING SYMPTOMS AMONG ADOLESCENT SEXUAL MINORITY GIRLS.

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Aims: Lesbian, gay, and bisexual adolescents are at risk of alcohol, cigarette, and marijuana use, particularly sexual minority girls (SMGs); however, little is known about polysubstance use among SMGs. We examined polysubstance use patterns among SMGs and heterosexual girls and their associations with mental illness using cross-sectional data.
Methods: Mixture modeling described patterns of past year alcohol, cigarette, and marijuana use in a sample of urban adolescent girls (Pittsburgh Girls Study; N=2064; mean age=17). Approximately 8% endorsed a lesbian or bisexual identity. Membership in each substance use class was predicted by sexual orientation, internalizing symptoms (i.e., depression, anxiety), and externalizing symptoms (i.e., conduct problems, oppositional defiant disorder). Substance use was also examined as a predictor of mental health profiles identified in mixture models.
Results: SMGs exhibited various use patterns: low substance use (61%), marijuana use (6%), cigarette use (14%), alcohol use (8%), and polysubstance use (12%). SMGs were at an increased risk for polysubstance use (OR=6.69, p<.001), cigarette use (OR=6.26, p<.001), and marijuana use (OR=3.86, p<.001) relative to heterosexual girls. The disparities remained after controlling for mental health symptoms. Specifically, externalizing, but not internalizing, symptoms independently predicted polysubstance use over and above sexual orientation.
More than one-third (36%) of SMGs exhibited normative mental health, but some were at risk of externalizing (8%) or internalizing (23%) symptoms, or a combination of both (14%). Substance use consistently predicted externalizing symptoms and co-occurring internalizing and externalizing symptoms.
Conclusions: Substance use interventions for SMGs may benefit from targeting risk factors that cut-across several substances, such as externalizing symptoms.
Financial Support: NIDA R01 DA030385, NIDA R01 DA012237, NIMH R01 MH056630.

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DOES EFFECTIVE COMBINED PREVENTION REDUCE RACIAL/ETHNIC AND SEX DISPARITIES IN HIV INFECTION AMONG PWID.

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Aims: Significant racial/ethnic disparities in HIV infection among persons who inject drugs (PWID) exist in many areas, with ethnic minority group members usually having higher HIV prevalence. "Combined" prevention programming has greatly reduced HIV transmission among PWID. We examined ethnic disparities in HIV infection among PWID in New York City over 30 years of HIV combined prevention programming.
Methods: Qualitative interviews and HIV testing were conducted among PWID entering Beth Israel drug treatment programs 1990-2012. Comparisons were made for two periods: 1990-1994, with methadone treatment, community outreach, and HIV testing, vs. 2007-2012, full "combined" prevention, with syringe exchange, ART and condom social marketing.
Results: 7139 subjects were recruited from 1990-2012. HIV prevalence declined among all major racial/ethnic groups from 1990-1994 to 2007-2012: among Whites from 27% to 3%, among African-Americans from 57% to 24%, among Latino/as from 53% to 12% (all $p < 0.01$). The greatest percentage reduction in HIV prevalence (89%) occurred among Whites, with a 58% reduction among African-Americans and a 77% reduction among Hispanics. Odds ratios for HIV prevalence among African-Americans compared to Whites were: 3.55 for 1990-1994 and 9.18 for 2007-2011. Odds ratios for HIV prevalence among Hispanics compared to Whites were 3.00 for 1990-1994 and 3.96 for 2007-2011. There were no statistically significant changes in the disparity odds ratios over time, and the direction of odds ratio changes were towards higher disparities over time.
Conclusions: Cumulative implementation of combined HIV prevention programs for PWID has been followed by substantial reductions in HIV prevalence among all major racial/ethnic groups, but large disparities persist. White PWID in NYC are close to an "AIDS free generation" while African-American and Hispanic PWID are still far from this goal. The potential for current interventions to reduce disparities will be critically examined.
Financial Support: Grant Funding: 5R01DA003574

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GENDER DIFFERENCES IN PSYCHIATRIC SYMPTOMS AMONG OPIATE-DEPENDENT PATIENTS IN RUSSIA.

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Aims: The current study explored potential gender differences in psychiatric symptoms among opiate dependent patients entering Naltrexone treatment in Saint Petersburg, Russia.
Methods: Participants were 180 treatment seeking adults (121 males; 51 females) who had enrolled in a randomized clinical trial examining pharmacological and behavioral counseling interventions for drug abuse and HIV risk reduction. All participants met DSM-IV criteria for opiate dependence. Baseline psychiatric symptoms were assessed using the Brief Symptom Inventory (BSI; 1983).
Results: Independent samples t-tests indicated that females were significantly higher than males on the depression subscale ($p < .01$), anxiety subscale ($p < .05$), and general severity index (GSI; $p < .01$). Males and females did not differ significantly on demographic variables (e.g., age, education) or on other BSI symptom dimensions.
Conclusions: Findings indicate that opiate dependent females in Russia report greater depression, anxiety and overall psychological distress symptoms than opiate dependent males. Given that gender differences in treatment response among opiate dependent patients have often been found, findings may have important implications for developing gender-specific treatments. Benefits of clinical interventions for opiate dependence among Russian females might be improved by addressing co-occurring depression and anxiety symptoms among these individuals.
Financial Support: Supported by a NIDA grant (R01 DA027405; PI Chawarski).

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SELF ADMINISTRATION OF OXYCODONE BY ADOLESCENT AND ADULT MICE DIFFERENTIALLY AFFECTS HYPOTHALAMIC MITOCHONDRIAL METABOLISM GENE EXPRESSION.

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Aims: Illicit prescription drug use among adolescents is a pressing public health concern; 12% of high school students report using prescription opiates with many progressing to use heroin. However, little is known of the effects of prescription opioids on the adolescent brain compared with the adult brain. The hypothalamus is involved in regulating feeding, reproduction and stress-induced drug seeking behavior. Therefore, this study examined the effect of adolescent oxycodone self administration on gene expression related to hypothalamic mitochondrial energy metabolism.
Methods: Adolescent and adult mice self-administered oxycodone (0.25mg/kg/infusion) or served as saline controls 2 hours daily for 14 days. The mRNA from the hypothalamus was analyzed with a "mitochondrial energy metabolism" qPCR array with 84 genes.
Results: The mRNA levels of ubiquinol-cytochrome c reductase, complex III subunit VII showed an experiment-wise significant increase (permutation test accounting for multiple variables) in adolescent mice that self administered oxycodone as compared with controls. This effect was not seen in the adults. MRNA levels of oxidase assembly 1-like showed a point-wise significant decrease in adult mice that self administered oxycodone. A Student's T-test showed 27 genes had increased expression in adolescents that self administered oxycodone. In adults, 8 genes had lower expression; none showed higher expression.
Conclusions: This shows that prescription opiate use caused significant changes in mitochondrial metabolism gene expression. The age group differences show the importance of studying adolescents in order to create effective treatments.
Financial Support: Work supported by NIH-NIDA 1R01DA029147 (YZ) and the Adelson Medical Research Foundation (MJK)

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IS OPIOID DOSE A STRONG PREDICTOR OF THE RISK OF OPIOID OVERDOSE?: IMPORTANT CONFOUNDING FACTORS THAT CHANGE THE DOSE-OVERDOSE RELATIONSHIP.

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Aims: Recent studies have reported higher opioid overdose risk at higher opioid doses, and have been used to suggest employing restrictions on patient access to analgesic doses >100mg/day morphine equivalent dose (MED). However, these studies did not explore the dose-risk relationship above 100mg/day MED or adjust for several potential confounders, eg, use of immediate-release vs. extended-release opioids, which have different indications, use of sedative/hypnotics (SH), and psychiatric or substance use disorders (SAD). Therefore, we assessed the opioid dose-overdose relationship adjusting for these variables across the range of opioid doses used in clinical practice.
Methods: Adults with a new opioid dispensing were identified in the MarketScan Commercial dataset (01/2008-03/2012) and were followed until first of: overdose (ICD-9-CM codes: 965.00, 965.02, 965.09), insurance enrolment discontinuation, or end of study period. Daily opioid exposure and person-years (PY) for all patients was categorized (1-19 to ≥350mg/day MED).
Results: In 9.6 million individuals dispensed a new opioid, 3,224 cases of overdose were identified during 14 million PY, including 585,000 PY of opioid exposure, 90% at <100mg/day MED. The overall overdose incidence was 0.02 cases/100PY. The crude incidence of overdose increased with opioid dose, from 0.13%/year (1-19 mg/day) to 1.08%/year (≥350mg/day). The crude RR for ≥350mg/day vs. 1-19mg/day was 8.37 (95%CI 6.18, 11.33) while the adjusted RR was 2.05 (1.46, 2.88). The adjusted model included strong predictors of overdose (opioid type, SH use, age, psychiatric diagnoses, SAD) and gender. In the adjusted model, the highest risk of overdose was observed at 50-99mg/day vs. 1-19mg/day (incidence rate=2.80 [2.34, 3.34]; risk did not increase significantly above 100mg/day.
Conclusions: These results suggest that opioid dose is not a strong independent predictor of overdose risk, while other factors are. Restricting patient access to <100mg/day MED may not be the best criterion to enhance the benefit-risk ratio of opioid use in the community.
Financial Support: Purdue Pharma LP

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CHANGES IN ATTENTIONAL BIAS TO DRUG CUES AND FMRI STROOP WITH BEHAVIORAL TREATMENT FOR COCAINE DEPENDENCE.

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Aims: Poor cognitive control and attentional bias to drug cues may contribute to the maintenance of substance use disorders. Cognitive behavioral therapy may exert its effects in part through targeting these processes.
Methods: Cocaine-dependent individuals were randomized to 8-weeks of outpatient treatment as usual (TAU) or TAU plus computer based cognitive behavioral therapy (CBT4CBT). At pre- and post-treatment, participants completed an out-of-scanner Drug Stroop - a measure of attentional bias to drug-related stimuli. A subset also completed a functional magnetic resonance imaging (fMRI) Color-Word Stroop, a measure of cognitive control.
Results: Participants (N=61) had diminished Drug Stroop Effect (less slowing to drug vs neutral) at post- vs pre-treatment. A treatment X trial type X time interaction indicated more change in Drug Stroop Effect in CBT4CBT vs TAU from pre- to post-treatment. When splitting participants by whether they attained 3+weeks continuous abstinence during treatment, a similar interaction indicated patients who achieved longer abstinence changed more in Drug Stroop Effect from pre- to post-treatment.
Pre-treatment fMRI Color-Word Stroop correlated with cocaine use during treatment (N=24). Stroop-related activity was higher at pre- vs. post-treatment in regions implicated in cognitive control.
Conclusions: Drug Stroop findings were consistent with diminished attentional bias to drug-related stimuli following treatment, particularly among individuals who received CBT4CBT or achieved 3+weeks abstinence. fMRI Stroop results of diminished Stroop-related activity at post- vs pre-treatment replicated our previous findings and may indicate improved efficiency of cognitive-control processes following treatment. Pre-treatment fMRI Stroop correlations with within-treatment cocaine use were consistent with relevance of cognitive control to treatment success. These findings suggest CBT4CBT and TAU may differentially affect cognitive control (including attentional bias to drug stimuli), which may relate to clinical outcomes.
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CARDIOVASCULAR SAFETY OF IBUDILAST TREATMENT WITH INTRAVENOUS METHAMPHETAMINE ADMINISTRATION.

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Aims: Methamphetamine (MA) dependence causes devastating personal and public health consequences. While there are effective behavioral therapies, no effective pharmacotherapy exists at this time. Combination treatment would likely reduce the growing public health burden. Given known MA-related cognitive dysfunction/degeneration, we tested a novel approach to pharmacologic treatment via suppression of MA-induced glial activation. We assessed the safety and tolerability of intravenous MA administration during treatment with ibudilast, a modulator of CNS glial activation.
Methods: Non-treatment seeking MA dependent volunteers (N=11) were hospitalized in an inpatient research unit for 28 days during which they received intravenous MA (0 mg, 15 mg, or 30 mg) during treatment with ibudilast (20 mg BID and 50 mg BID) and placebo using a randomized double-blind, placebo-controlled within-subjects crossover design. Peak change in heart rate and blood pressure following MA infusion under each ibudilast dose as well as reported adverse events were compared.
Results: There were no significant main effects for ibudilast on peak change in heart rate, systolic, or diastolic blood pressure nor were there any significant interactions between ibudilast and MA. Reported adverse events were similar during ibudilast- and placebo- treatment, and were typical adverse events observed during MA studies. Expected stimulant cardiovascular effects (increased heart rate, systolic blood pressure, diastolic blood pressure) were associated with MA administration, with the higher MA dose associated with greater increases in all 3 cardiovascular measures.
Conclusions: Ibudilast treatment was well-tolerated with MA administration. Cardiovascular effects of MA were not significantly altered with ibudilast treatment. This initial phase I study supports the safety and tolerability of ibudilast for treatment of MA dependence and provides evidence to further study the efficacy of ibudilast.
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INCREASING ACCESS TO OPIOID AGONIST TREATMENT IN U.S. TREATMENT SHORTAGE AREAS.

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Aims: The overall number of physicians waivered to prescribe buprenorphine has been increasing. However, there is little information about their location and whether their distribution increases access to opioid agonist treatment in communities where opioid treatment programs are scarce. We sought to examine the extent to which geographic distribution of buprenorphine-waivered physicians has enhanced access to opioid treatment.
Methods: Using data from the Buprenorphine Waiver Notification System, NSSATS, the Area Resource File, the DEA's System to Retrieve Information from Drug Evidence, and the National Vital Statistics System, we adopted a standardized approach used in identifying communities with health professional shortages, and identified counties that had a shortage of waivered physicians, opioid treatment programs, and opioid treatment over all.
Results: The percentage of counties with a shortage of opioid treatment programs changed from 90% in 2002 to 87% in 2009. However, the percentage of counties with a shortage of waivered physicians fell from 99% of counties in 2002 to 51% in 2009. The percentage of the population living in counties with a shortage of opioid treatment programs fell modestly. However, the percentage of counties with a shortage of waivered physicians decreased so that only 13% of the population resided in a treatment shortage county in 2009.
Conclusions: The expansion of waivered physicians has the potential to substantially expand access to opioid agonist treatment. There are large parts of the county in which access to opioid agonist treatment remains limited. Policies aimed at increasing the number of physicians waivered for prescribing buprenorphine in communities without methadone clinics might be an effective strategy for increasing treatment capacity, particularly in areas with limited access to opioid treatment programs.
Financial Support: This work was supported by NIDA 1R01DA032881-01A1.

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THE DIFFERENTIAL ROLE OF EXECUTIVE DYSFUNCTION ON HIV RISK BEHAVIORS AMONG AFRICAN-AMERICAN DRUG USERS.

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Aims: The present study sought to test whether African American male and female drug users differed in rates of executive dysfunction and the degree to which executive dysfunction is associated with elevated HIV risk behavior.
Methods: A series of secondary data analyses were conducted on data from African American drug users (N = 453; M age = 38.24, SD=9.1) enrolled in the NEURO Epidemiologic Study of HIV in Baltimore, MD. Participants were recruited through street outreach and administered a standardized HIV Risk Behavior Interview and a neuropsychological battery.
Results: On the Wisconsin Card Sorting Test (WCST), females showed a greater rate of impairment in total errors (Adjusted Odds Ratio [AOR]=1.65, 95% Confidence Interval [CI]: 1.04-2.63, p=.034) and preservative errors (AOR=1.56, 95% CI: .99-2.45, p=.05) when compared to males. They also exhibited a significantly higher rate of dysfunction on Tower of London (TOL) total move score (AOR=1.96, 95% CI: 1.27-3.04, p=.003), execution time (AOR=2.24, 95% CI: 1.45-3.48, p=<.001) and total time (AOR=2.13, 95% CI: 1.37-3.3, p=.001). In addition, women with impairments on WCST preservative errors were significantly more likely to engage in sex trade for money compared to those with intact WCST preservative error scores (AOR=1.95, 95% CI: 1.03-3.68, p=.041). Impairment on TOL execution time was a significant predictor of infrequent condom use among women (AOR=3.42, 95% CI: 1.37-8.54, p=.008). Conversely, executive impairment on WCST or TOL did not predict increased HIV risk behaviors among men.
Conclusions: Our findings indicate that African American female drug users are more likely than African American males to exhibit frontal-executive deficits. Additionally, these deficits are significant risk factors for HIV-risk behavior among females. Thus, HIV prevention efforts should consider gender-specific interventions that focus on cognitive executive skills training.
Financial Support: This research was funded by NIDA R01 DA14498.

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INHIBITORY CONTROL IN PATIENTS WITH COCAINE ABUSE IS EQUALLY DISRUPTED BY GENERIC AND PERSONALLY SALIENT COCAINE IMAGES.

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Aims: To determine the extent that salient cocaine cues increase breakdown of control in patients with cocaine abuse, we measured control over behavior in a task where patients must inhibit an impulsive action and instead look away from a suddenly appearing image. Cues were personally salient cocaine or neutral stimuli (participants handled them and rated their craving; photos of them touching the cues were used during the task) and generic cocaine (photos of cocaine-related cues) and neutral stimuli.
Methods: Twenty-five treatment-seeking patients (M= 37.2 yrs; 19 males) with a history of cocaine abuse (M= 14.6 yrs) and use of cocaine within the last month (16.2 days of use) were inducted into the study. Initial assessments included Voris cocaine craving measures and anti-saccade performance.
Results: Voris craving scores were significantly higher (t= 5.82, p< .0001) after handling the cocaine cues (M= 27.3) than after handling the neutral cues (M= 13.3). Inhibitory control was significantly worse (t= 2.1, p< .05) for the salient cocaine cues (M= 37%) than the salient neutral cues (M= 33%). Likewise, errors were significantly higher (t= 2.8, p< .01) for the generic cocaine cues (M= 34%) than the generic neutral cues (M= 29%). Importantly, there was no hint of a statistical (t<1) or numeric difference in breakdowns in inhibitory control between generic cocaine cues (Mean difference of drug-neutral = 5%) and salient cocaine cues (Mean difference of drug-neutral = 4%).
Conclusions: Both types of drug cues caused significant breakdowns of inhibitory control. Handling cocaine cues significantly increased patients craving scores; however, these salient drug cues did not induce increased breakdowns in inhibitory control. Preliminary results suggest that personalized and generic drug cues are equally harmful in causing breakdowns of control suggesting a general bias toward drug cues. Neuroimaging studies are underway to test the underlying neural circuitry.
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UNDERSTANDING THE BUZZ ABOUT ENERGY DRINK USE IN COLLEGE STUDENTS.

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Aims: There has been a dramatic increase in the use of energy drinks (ED), especially among college students. These drinks frequently contain the equivalent of 3-5 cans of soda in a single ED, and they have been associated with problem behaviors including increased alcohol use, drug use, risky sexual behavior, and other risk-taking behaviors. To further prevention and intervention programs for caffeine-associated problem behaviors, it is critical to identify those students most likely to use ED and have problems associated with their caffeine use. This study examined associations between ED use, demographics, personality type, antisocial behavior, and peer group deviance in a sample of college students.
Methods: N=2056 college freshmen from a large, urban university in Virginia completed an online survey, "Spit for Science". The primary study examined interactions between genetic, environmental, and developmental factors that influence health-related outcomes in college students.
Results: Participants were 18.5 years old (SD=0.47), primarily female (60%), and Caucasian (51%). Nearly one-fifth (18%) reported ED use, males more often than females (21% vs 16%, p=0.005). Female ED users were significantly less conscientious than non ED (NED) users (p=0.007), Also, female ED users reported significantly more antisocial behavior, peer group deviance, phobic anxiety, and depression than NED users (all p≤0.01). Male ED users were significantly more extroverted than male NED users (p=0.012). A regression analysis found that increased extroversion, decreased conscientiousness, and increased peer group deviance were independently associated with increased ED use.
Conclusions: The data from the current study suggest that there are some identifiable traits associated with ED use, and these traits are different between female and male college students. Interventions targeting students with specific characteristics may be useful to affect adverse health behaviors associated with ED use in college students.
Financial Support: NIH R37 AA011408

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SYNTHETIC CANNABINOID USE AND AWARENESS IN A DRUG ABUSE TREATMENT CLINIC.

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Aims: Synthetic cannabinoids (SC) present unique challenges to drug treatment programs because they are difficult to detect, the exact substances contained in products are not known and frequently change, and staff are not always aware of or discussing use of these products with their patients. This pilot study examined use and awareness of SC as among patients and counseling staff in an urban Baltimore drug abuse treatment program.
Methods: 27 patients and 8 clinical staff members were anonymously surveyed via computer in a private location.
The patients were a primarily low-income (25/27 disabled or unemployed), African-American (21/27), heroin and cocaine-using population. (23/27 had problems with heroin and 22/27 with cocaine.) They had an average of 5.1 previous drug treatment episodes, and the majority reported a co-occurring mental health diagnosis (25/27).
Results: 46% of these patients (13/28) endorsed having been offered a SC product, and 14% (4/28) had used an SC. Half of those with SC use history indicated that one motivation for use was that SCs provided them the ability to get high without being detectable in urine drug tests. Users were evenly divided among males and females and Caucasians and African-Americans. Prior use of an SC was associated with also having been a cigarette smoker and having had problems with alcohol. Only one had endorsed having had a previous cannabis use disorder.
Counselors, who reported an average of 17 years experience, estimated that about half of all clients at the clinic had used an SC, but that they do not routinely address use of these substances with their patients. Most counselors only discussed SCs if the client brought it up first, or "only with certain clients" who they felt fit the profile of users.
Conclusions: These results suggest that while use is not yet widespread in this population, the use of synthetic cannabinoids is a potential source of undetected clinical impairment, and that surveillance should increase, even in populations not conventionally considered to be at risk for use of these substances.
Financial Support: NIDA grant DA023186

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TREATMENT OF WOMEN WITH SUBSTANCE USE DISORDER AT HIGH RISK OF STIGMATIZATION.

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Aims: The study focuses on evaluation of treatment of traumatized substance use disorder mothers at risk of stigmatization. Pregnant women with substance use disorder have significant comorbidities and PTSD and in fact represent a high risk group for stigmatization and exclusion from society. In the Czech Republic reports indicate a prevalence of 1.8% of illicit drug use among pregnant women from over one million mothers between 2000 and 2009. However, questions regarding pregnant women with substance use disorder in the Czech Republic requires further characterization, increased accuracy in reporting and determination of risk factors.
The Center for Family for women and pregnant women, part of the the Drop In Center, manages a comprehensive system for those with substance use disorder. Treatment is based on phases including minimal threshold, tasks and growth. Some of the women are in abstinence, some still use drugs or are in substitution treatments. The program is realized by a multidisciplinary team applying different methods such as cognitive behavioral approach, obsteric counseling or family skills.
Methods: This retrospective study was qualitative and quantitative and included case management and complex screening of the women. The cohort formed mothers in treatment for two years in a structured three phase program
Results: The study demonstrated that treatment program with maternal skills improved life skill competence and decreased the risk of loss of children to homes, supported continued employment and education.
Conclusions: The comprehensive three phase treatment program increases quality of life of women through preventing social exclusion and stigmatization.
Financial Support: no financial support

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MODULATION OF MICRORNA EXPRESSION IN THE AMYGDALA BY BINGE COCAINE AND WITHDRAWAL.

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Aims: MicroRNAs are short non-coding RNAs that regulate gene expression. We hypothesize that addiction relapse is influenced by interactions between addiction related neuroadaptations and stress response partially mediated by miRNA expression. Thus, we aim to study the effects of binge cocaine and withdrawal on miRNA expression in the amygdala, and alter in vivo expression of specific miRNA species to test the effects on drug seeking behavior.
Methods: Male SD rats received 15mg/kg/day of saline or cocaine for 10 days, and were sacrificed one hour or 25 hours after the last injection. Total RNA was isolated from amygdala, and hybridized to Affymetrix miRNA 3.0 chips containing all known miRNAs.
Results: We identified 76 miRNAs showing 2 fold change in expression in binge cocaine or withdrawal animals relative to saline. 38 miRNAs showed 2 fold change in expression in response to binge cocaine, and 47 after withdrawal from binge cocaine. Of the 76 miRNAs identified, 30 have been shown to regulate genes involved in drug addiction, and 26 are predicted to regulate genes involved in stress response. 11 miRNAs are predicted to regulate genes involved in both drug addiction and stress response. qRT-PCR validation is underway for 2 of these miRNAs (miR-214 and miR-375). Further, miR-218 and miR-34a, differentially regulated by binge cocaine and withdrawal are being validated by qRT-PCR. Downstream protein targets have been predicted for these miRNAs, and will be validated by western blot analysis.
Conclusions: We have identified 76 miRNAs that are regulated by chronic cocaine and withdrawal in the amygdala of male SD rats. 11 of these regulated miRNAs are known to be involved in responding to drugs of abuse, and are predicted to target proteins involved in stress response. These studies have the potential to further elucidate the etiology of drug addiction and relapse, and may provide promising targets for more effective therapeutic treatment of substance abuse.
Financial Support: T32 DA007237
P30 DA013429

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NICOTINE ALTERS BEHAVIOR IN PRE-ADOLESCENT RATS.

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Aims: While cigarette smoking has gone down among the adult population, a substantial number of young children continue to experiment with cigarettes and alternative tobacco products. The work by DiFranza et al reports that young children (6th graders) demonstrate a loss of autonomy following brief exposures to smoking. We hypothesized that brief nicotine exposures would alter behavior in young Sprague-Dawley rats
Methods: We examined the effects of a range of nicotine doses on 1) conditioned place preference (CPP) in 25 day old rats following both one and two exposures, 2) behavior on the elevated plus maze (EPM) 5 days following the second nicotine dose and 3) activity/ amphetamine challenge 7 days following the second nicotine dose. For data derived from 120 rats, mixed linear models were constructed for nicotine dose (0, 0.05, 0.5 mg/kg), sex, shipping/vivarium reared as independent variables with litter as a random factor.
Results: For CPP after 1 nicotine dose, there was a main effect of dose and a sex x dose interaction since nicotine increased CPP (time on drug side post-pre conditioning) more dramatically in females than in males. Following the second dose of nicotine, both doses increased time on the drug side compared to the 0 dose. Five days following the last dose, time on the open arm of the EPM showed a significant sex x dose interaction with marginally significant post-hoc tests. Seven days following the second dose of nicotine, baseline activity was significantly increased in males that received nicotine but not in females. There were no effects of previous nicotine exposure following amphetamine challenge.
Conclusions: Therefore, these results show that while nicotine does produce CPP in pre-adolescent rats, it also alters behavior 5 to 7 days later. These changes in behavior may relate to changes in behavior seen in young children following brief exposures to smoking which have been considered as precursors to smoking dependence.
Financial Support: Supported by SUNY Downstate.

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EFFECTS OF ALCOHOL INTAKE ON BALANCE AND STABILITY IN OLDER ADULTS: A PILOT STUDY.

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Aims: Little is known regarding the acute effects of small doses of alcohol on balance and stability, functions highly associated with falling, in older adults. Our study assessed balance and stability after acute intake of a low to moderate dose of alcohol in adults age >65 years.
Methods: After being screened and consented, 23 age-and-gender-matched, healthy, current drinkers age >65 were given approximately two standard alcoholic drinks adjusted to weight. Balance and stability were measured in 4 conditions – normal surface with open and closed eyes and padded surface (to reduce tactile input and challenge balance) with open and closed eyes. Limits of stability (LOS) were assessed using the Bertec Force Plate at baseline, i.e., prior to alcohol intake, and at 40 minute-intervals up to 160 minutes after alcohol intake.
Results: In this group of age-and-gender matched subjects, we found no statistical differences in BMI, number of weekly drinks, and assessments of liver function including AST and ALT between men (n=11) and women (n=12). The peak breath alcohol concentrations (BrAC) at 40-minutes post-alcohol ingestion were 0.032% and 0.030% for women and men, respectively. Overall, after adjusting for age and timepoint, higher BrAC in women was significantly associated with declined performance in normal open-eye condition ($p=0.02$), and in LOS ($p<0.0001$), whereas it had no effect in men.
Conclusions: Our preliminary data indicate that low to moderate alcohol intake may negatively affect balance and stability in older women, yet may be negligible in men. More research is needed to replicate the study results.
Financial Support: None

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BASAL NEUROENDOCRINE STATUS AND COCAINE CRAVING MEASUREMENTS IN ACTIVE COCAINE-DEPENDENT VOLUNTEERS AT ADMISSION AND AFTER 8 WEEKS OF ABSTINENCE.

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Aims: To examine the effect of 8 weeks of cocaine abstinence on neuroendocrine status and subjective cocaine craving in cocaine dependent volunteers.
Methods: Sixteen male and female active cocaine dependent subjects were admitted to the stress-minimized inpatient unit at the Rockefeller University Hospital for an 8-week abstinence study. Following admission, subjects completed the Cocaine Craving Questionnaire and baseline neuroendocrine testing, where blood was sampled for ACTH, cortisol and prolactin, from just prior to a saline placebo i.v. administration and 0-90 min thereafter. Subjects lived on the research unit during the 8-week study period, and were accompanied to an off-site substance abuse counseling program three times per week. Nine of the sixteen subjects were able to complete the entire 8 week protocol, at which time a 2nd saline placebo day and CCQ were obtained Seven of the sixteen subjects withdrew or were terminated from the study prior to completing the 8 weeks. Area under the curve (AUC) for ACTH, cortisol and prolactin was calculated and analyzed for all subjects at admission, and 8 weeks later for those completing the study.
Results: No significant neuroendocrine differences were found between subjects completing vs. subjects unable to complete the 8 week study. In completers, subjective measures of cocaine craving (CCQ scores) significantly decreased after 8 weeks of inpatient abstinence; however, no differences were seen in plasma ACTH, serum cortisol or prolactin levels between week 0 and week 8.
Conclusions: These results suggest that subjective measures of cocaine craving as measured by the CCQ decreased over a period of abstinence under stress-minimized conditions. Of interest, these time-dependent decreases in CCQ scores were not accompanied by changes in stress-responsive hormone levels in this 8 week abstinence period.
Financial Support: NIH-NIDA P50-DA005130 (M.J.K.), NCATS # UL1-TR000043 and The Adelson Medical Research Foundation.

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TOTAL RECALL?: RESEARCHERS' PERCEPTIONS OF THE CONSENT PROCESS.

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Aims: Research demonstrates participants' limited recall of essential information communicated during the consent process. Despite federal recommendations that consent information should be adequately recalled over the course of a study, many researchers have not adopted these recommendations. This study examined substance abuse researchers' perceptions of the informed consent process and the type of strategies they use to ensure recall of consent information.
Methods: We developed a 19-item web-based survey to assess (1) investigator characteristics, (2) area of research, (3) perceptions about the importance of consent recall, (4) beliefs about how well participants recall consent information, and (5) strategies they use to improve recall. To identify our sample, we conducted a search of the NIH RePORTER database. We identified 723 currently-funded NIDA and NIAAA investigators who conducted research requiring informed consent. We sent a link for the web-based survey to the identified sample. A total of 263 individuals responded (35% response rate) and 233 indicated they conducted human subjects research and were eligible for the survey. Respondents were entered into a drawing for a $200 Amazon gift card.
Results: The majority of respondents conducted experimental behavioral research with vulnerable populations. Most felt it was "very" (63%) or "somewhat" (31%) important for participants to recall consent information throughout the study. The majority felt that participants were only "moderately" able to recall consent information. The most commonly used consent strategies were providing copies of consent form (92%), regularly reminding participants of consent information (58%), and using consent quizzes (30%).
Conclusions: Although most researchers reported that ongoing consent recall was important, most believed their clients were not able to completely recall this information. In addition, they generally reported using only the most basic consent strategies. These findings support the need for broader implementation of empirically-based strategies to improve consent recall in substance abuse research.
Financial Support: Funded by NIDA grant R01-DA021621.

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DRINKING DURING THE FIRST TWO WEEKS OF A CLINICAL TRIAL SIGNIFICANTLY PREDICTS DRINKING AT THE END OF THE TRIAL.

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Aims: There is a robust association between early abstinence from drugs/cigarettes and long-term abstinence. This study evaluated whether this association was also true for alcohol. A secondary analysis of the COMBINE data was conducted to evaluate whether any self-reported drinking during the first 2 weeks of an alcohol treatment trial significantly predicted drinking at the end of the 16-week study.
Methods: Participants who specified abstinence as a treatment goal and who completed the 16-week intervention were dichotomized into early abstainer (N=440) and early drinker (N=418) groups based on whether they reported 1 or more drinks during the first 2 weeks of the trial. Drinking was evaluated as number of drinking and heavy drinking days.
Results: Participants were 74% Caucasian and 72% male. Overall, 25% of participants did not drink at all during the study. Early drinkers were more likely to report drinking (100% vs. 52%, p<.001) and heavy drinking (91% vs. 40%, p<.001) during weeks 3-16 compared to early abstainers, respectively. Drinking during the first 2 weeks was significantly correlated with drinking (p<.001) and heavy drinking (p<.001) on the final day of treatment. These results were further supported by multivariate logistic regressions that controlled for treatment group, treatment site, and gender, which revealed that drinking and heavy drinking during the final week of treatment was 3.6 (p<.001) and 3.2 (p<.001)-fold more likely, respectively, among early drinkers vs. early abstainers. Finally, early drinkers reported resuming drinking (4.4 vs. 23.2 days; p<.001), and heavy drinking (10 vs. 20 days, p<.001) more quickly compared to early abstainers.
Conclusions: Overall, these data indicate that alcohol use within the first 2 weeks of a treatment trial is highly predictive of drinking and heavy drinking throughout the trial and at the end of the study. This information can be used to identify patients for whom additional resources and support may be needed early in their treatment, and may help increase the efficacy of alcohol treatment interventions.
Financial Support: Supported by DA023186.

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ADHD AS RISK FACTOR FOR EARLY ONSET AND LATER SEVERITY OF ILLICIT SUBSTANCE USE: AN ACCELERATED GATEWAY MODEL.

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Aims: The primary study aim was to assess history of ADHD as a risk factor for early onset of drug use and severity of current drug use among adult heroin and cocaine users. It was hypothesized that adult drug users with a history of ADHD would display a similar pattern of initiation but with an earlier age of onset compared to drug users without ADHD.
Methods: A secondary data analysis of participants enrolled in the NIDA-funded NEURO-HIV Epidemiologic Study in Baltimore, Maryland. The sample included 984 current drug using adults (M age=35.3, SD=9.8; 51.9% male; 61.4% African American). Participants were community recruited and completed an HIV-risk behavior interview. Chi-square and independent t-test analyzed demographics and drug use behaviors between ADHD and non-ADHD groups. Logistic regressions assessed gender differences in the association of ADHD and heavy smoking.
Results: ADHD history was endorsed by 135 (13.7%) participants, with males being more likely to report a diagnosis (males = 16.4%, females = 10.9%). Individuals with ADHD were significantly younger, more likely to be male, and more likely to be Caucasian. As hypothesized, the ADHD group reported a significantly younger age of onset for all substances (cigarettes, alcohol, marijuana, cocaine, and heroin). Mean differences in age of onset ranged from 1.5 years (marijuana) to 2.7 years (injection cocaine). Participants with a history of ADHD were also significantly more likely to be current heavy cigarette smokers (X2=15.4, p<.001), marijuana users (X2=14.25, p<.001), and heroin and/or cocaine injectors (X2=6.98, p=.008). There was a significant relationship between heavy smoking and ADHD in females only, after adjusting for drug use and demographics (AOR=3.37, 95%CI: 1.04-10.95, p<.05).
Conclusions: ADHD may result in an accelerated gateway to substance use and should be an important consideration for drug use prevention and intervention efforts.
Financial Support: This project was supported by NIDA R01DA14498.

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SUBSTANCE USE AND SEXUAL RISK AMONG MEN WHO HAVE SEX WITH MEN AND WOMEN AND THEIR FEMALE PARTNERS.

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Aims: We aim to explore drug use, sex risk, and biologically-confirmed STI/HIV among both MSMW and their female partners.
We hypothesize that MSMW and their female partners will have elevated levels of drug use, sex risk, and infection.
Methods: The Network, Norms and HIV/STI Risk among Youth (NNHRAY) study collected sociometric network data and specimens for STI/HIV testing from 2002-2003. Current analyses were restricted to respondents involved in at least 1 sexual partnership in the past 3 months for which interview data for both members of the partnership were available (N=182 men, 161 women). We evaluated drug use, sex risk, and biologically-confirmed STI/HIV in MSMW (men who had sex in the past 3 months with male and female partners) and their female partners (women who had sex in the past 3 months with an MSMW). Reference groups are men who have sex with women only and their sex partners.
Results: MSMW, versus men who have sex with women only, had 30 to 50% increased odds of non-injected heroin, cocaine, and crack use and had over twice the odds of multiple partnerships, five times the odds of sex trade, six times the odds of HIV infection, and over 1.5 times the odds of other STI; elevated levels of these outcomes were comparable to men who have sex with men only (MSMO). Female partners of MSMW versus women whose partners had sex with women only (the referent) had approximately twice the odds of non-injected heroin use, crack use, and injection drug use and 1.5 to 2 times the odds of multiple partnerships, sex trade, and HIV infection.
Conclusions: Interventions should address the bidirectional nature of risk within male and female partnerships of MSMW.
Financial Support: This study was supported by: R01 DA13128, R01 DA-028766, R25 MH-080644 and NIMHD LRP. This abstract does not necessarily represent views of NIDA, NIMH or NIMHD.

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THE IMPACT OF PRESCRIPTION OPIOIDS ON CD4 COUNT IN HIV: A LONGITUDINAL ANALYSIS.

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Aims: Opioids have immunosuppressive properties and are commonly prescribed for pain to HIV-infected (HIV+) patients. We sought to determine whether prescription opioids impact HIV disease progression.
Methods: We conducted a longitudinal analysis among HIV+ patients in the Veterans Aging Cohort Study (VACS) from 2006 to 2010. CD4 cell count was assessed at 6-month intervals. Mean daily morphine equivalent dose (MED) based on prescribed outpatient opioids was determined during each corresponding interval. Long-term opioid receipt was defined as > 90 days in a given year. Covariates were demographics, comorbidities and VACS Index score (validated prognostic biomarker index), smoking status, and pain. Substance use was characterized using self-report of illicit drugs, non-medical use of prescriptions and the AUDIT. We controlled for time-updated receipt of immunosuppressive medication (e.g., steroids) and antiretroviral therapy (ART). We used generalized estimating equations to assess the association between MED and CD4 cell count stratified by baseline ART use.
Results: Among 2020 HIV+ patients, 81% were on ART. MED was similar among those not on and on ART (median [IQR] = 21 [15, 31] vs. 22 [15, 39], p=0.25). Among those not on ART, 28% received >1 opioid and 6% had long-term receipt. Among those on ART, 31% received >1 opioid and 10% had long-term receipt. Baseline median CD4 cell count was higher among those not vs. those on ART (429 vs. 397cells/cc3, p=0.02). For patients not on ART, each 10 mg increase in daily MED was associated with a 1.88 (95% CI -2.98, -0.78) adjusted decrease in CD4 cells/cc3 on average over time. For those on ART, there was no change in CD4 cells/cc3 associated with 10 mg increases in daily MED [0.74 (95% CI -1.75, 0.26)].
Conclusions: Prescription opioids are associated with a decrease in CD4 cell count among patients not receiving ART. Our findings support efforts to optimize ART use among patients requiring opioids.
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K2 USE AT COLLEGE ENTRY AND EXPERIMENTATION OVER COLLEGE CAREER.

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Aims: K2 ("spice") consists of an herbal blend of plant matter and chemical synthetic cannabinoids. K2 emerged in the early 2000s as a popular alternative to marijuana among youth and young adults. K2 use has been associated with adverse health effects, such as psychosis. As a consequence, there has been an increase in ED visits among this population due to use of K2. This study sought to identify factors that predict use of K2 prior to college and experimentation during college.
Methods: In fall 2010, 3,146 students at 11 colleges in North Carolina and Virginia were recruited to participate in a web-based longitudinal cohort survey, which included questions about use of K2. Random-effects logistic regression models were used to identify factors associated with lifetime K2 use at college entry and experimentation during college.
Results: 7.6% of students in the sample reported having used K2 prior to college, and 5.3% reported trying K2 since starting college (total lifetime prevalence of 12.9%). K2 use prior to college was associated with ever use of marijuana (AOR=10.6) and illicit drugs (AOR=3.1), smoking tobacco from a hookah in the past 30 days (AOR=2.4), high sensation seeking score (AOR=3.1), and low religious service attendance (AOR=0.6). Experimentation with K2 during college was associated with past 30 day alcohol use (AOR=2.9), smoking tobacco from a hookah in the past 30 days (AOR=4.0), higher sensation seeking score (AOR=1.7), and lower paternal education level (AOR=0.5). All significant at p<0.05 or less.
Conclusions: While K2 use at college entry and experimentation during college was associated with high sensation seeking scores and hookah use, K2 use prior to college entry was associated with lifetime marijuana and illicit drug use. Given the growing prevalence of K2 among college students, and substantial health consequences, college administrators should ensure that K2 is included in comprehensive prevention efforts.
Financial Support: This research was supported by Award Number R01CA141643 from the National Cancer Institute.

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WITHDRAWN

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DRUG USE AND RESPONSE TO ALCOHOL INTERVENTION AMONG HIV+ MEN AND WOMEN.

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Aims: HIV-infected patients face varied risks from heavy drinking. A recent study showed that a motivational interviewing session (MI) reduced drinking among HIV-infected heavy drinkers, especially when paired with daily self-monitoring via interactive voice response technology (IVR) (Hasin et al., 2013). However, many participants in this study used drugs (cocaine: 32.7%, marijuana: 32.3%; Elliott et al., under review), raising the question of whether drug users responded differentially to treatment. Also unclear was whether gender differences in drug use found in the general population applied to this high-risk group, and if gender impacted the influence of drug use on treatment. Therefore, we aimed to investigate: whether men and women differed in drug use, whether drug use affected response to treatment, and whether gender interacted with drug use in predicting response to treatment.
Methods: Participants were 254 HIV-infected primary care patients with past month binge drinking (78% male; 94.5% minority), completing one of three drinking interventions: MI, MI+IVR, or a DVD educational control. Drinking was assessed at end of treatment.
Results: Men and women reported similar rates of cocaine (32.8% vs. 32.1%; p=0.92) and marijuana (33.3% vs. 28.6%; p=0.50) use. Controlling for intervention condition and baseline drinking, cocaine use predicted more drinking whereas marijuana use predicted less drinking at end of treatment (ps<0.05). Further, marijuana use status interacted with intervention type (p<0.05), such that differential intervention efficacy was only found in nonusers. Gender did not predict drinking outcome, response to intervention type, or the effect of drug use on drinking.
Conclusions: Heavily drinking women with HIV use drugs at rates similar to men, and drug use impacts treatment in complex ways. These findings highlight the need to screen HIV-infected men and women for concurrent alcohol and drug use, given that drug use can affect treatment.
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NON-ETOH DRUG USE AMONG WOMEN IN OUTPATIENT TREATMENT FOR ALCOHOL DEPENDENCE.

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Aims: Aims: Gender differences in alcohol use disorders have led to the development of female specific treatments, but it is unclear if other drugs should be targeted in this sample as well. This study examined drug use lifetime patterns and in relation to drinking before and during treatment for alcohol dependent (AD) women.
Methods: Methods: 182 AD women completed an intake and 155 with no current psychotic symptoms or physiological dependence on other drugs were randomized to 12-sessions of individual or group CBT. Mean age was 49, income $85K, 89% Caucasian, 57% employed, and 48% married. Mean percent days drinking (PDD) and mean drinks per drinking day (MDPDD) pre-treatment were 66% and 7.3.
Results: Results: Among the 87% of women with lifetime use of at least one illicit drug class, including: 12% sedatives, 83% cannabis, 24% stimulants, 16% opioids, 50% cocaine, 30% hallucinogens. 80% of women reported lifetime use of nicotine. Mean age of heaviest lifetime use ranged from 20 to 31 across drug classes. At intake, 27 women had used at least one illicit drug class in the past month. Users of cannabis (n=26) or cocaine (n=10) in the past year drank less frequently (cannabis, t=2.3, p<.05; cocaine, t=3.32, p<.01) but at higher quantities (cannabis, t=-2.2, p<.05; cocaine, t=-3.8, p<.001) at baseline than nonusers. Daily smokers reported higher baseline MDPDD than intermittent smokers. Cannabis use in the past year was associated with less reduction in PDD during treatment (F=8.2, p<.01). Use of any illicit drug in the month prior to treatment entry was associated with less reduction in PDD (F=10.2, p<.01) and quantity (F=10.0, p<.01) during treatment.
Conclusions: Conclusions: This sample of women seeking treatment for AD reported substantial lifetime use of non-ETOH drugs that was associated with higher drinking intensity at baseline and poorer response to treatment for drinking, providing support for consideration of illicit drug or nicotine use in development of alcohol treatments for women.
Financial Support: Financial Support: This project was funded by NIAAA grant R01 AA017163.

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OPIOID DEATHS OR POLYDRUG/MULTI-CAUSE DEATHS?

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Aims: Overdose deaths involving prescription opioids have increased over the last decade. To promulgate effective, balanced policies and resulting actions aimed at reducing them while preserving access to medications for legitimate medical purposes, accurate characterization is necessary.
Methods: Methods: The 2010 Multiple Cause Mortality public-use files from CDC's National Vital Statistics System were used to evaluate contributing causes of death (CCOD) for drug-related deaths involving prescription opioids using both entity- and record-axis multiple condition codes. Other variables including age, sex, and manner of death were also analyzed.
Results: A substantial number of US drug-related death records involving prescription opioids also list other conditions or drugs/classes (licit or illicit) as CCOD. Consistent with recent CDC publications, ~30% of the 16,680 deaths involving prescription opioids also list a benzodiazepine as a CCOD. Additionally, over 2,000 of those deaths also list alcohol as a CCOD. On average, drug-related deaths involving an opioid list 4 CCOD (maximum of 15, including other drugs or medical conditions). While the large majority of deaths in the total 2010 database (⟩2.4 MM) list 3 or fewer CCOD, over 85% of the 5,025 deaths involving both benzodiazepines and opioids list between 4 and 8 CCOD. Consistent patterns emerged across all drug-, opioid-, and benzodiazepine-related deaths: the 45-54 age bracket had the largest frequency among 11 brackets; ~60% were male; and death certificates listed at least 2, but as many as 15 CCOD.
Conclusions: Multiple contributing causes are common in drug-related deaths involving prescription drugs, particularly with opioids and benzodiazepines. Potential interactions between these and other concomitant medications or co-morbid conditions should be highlighted in prescribing guidelines, provider educational initiatives, and by public health policies aimed at reducing prescription drug misuse and abuse. Results will be updated when 2011 data are available.
Financial Support: Full-time employees of Purdue Pharma L.P.

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PRELIMINARY RESULTS OF PROJECT EX IN SPAIN: A CLASSROOM-BASED SMOKING PREVENTION AND CESSATION PROGRAM.

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Aims: The latest studies confirm an increase of tobacco use in Spanish adolescents. Unfortunately, relatively few studies aimed to teen smokers have been conducted and evaluated compared to programs for adults. This study focus on the immediate outcomes of Project EX (Sussman & Lichtman, 2010), an evidence-based program for smoking cessation and prevention.
Methods: The original protocol was translated and culturally adapted to be applied to Spanish adolescents. The eight-session classroom-based curriculum was developed and tested 4 weeks after in a randomized controlled trial with 1,469 Spanish students randomly assigned to program and control conditions. Participants were aged from 14 to 21 years (M =15.26; SD = 1.20), 53.8% male.
Results: Students in the program condition showed greater increase of knowledge regarding tobacco (5.92%; p < 0.001) from pretest to posttest. Students in the program condition also experienced a reduction in daily (0.35 to 0.27), weekly (2.11 to 1.28) and monthly smoking (4.90 to 4; p = 0.05). They also reported favorable ratings of the program quality, and 80.4% of adolescents reported that Project EX helped them to strengthen its commitment to stay quit.
Conclusions: The classroom version of Project EX was effective for Spanish adolescents, as it has reduced the tobacco use and strengthened the commitment of non-smokers to continue being abstinent.
Financial Support: Supported by the Spanish Department of Economy and Competitividad (Ministerio de Economía y Competitividad Reference, PSI2011-26819)

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A COMPARISON OF YOUNG ADULTS SEEKING TREATMENT FOR CANNABIS AND OPIOID DEPENDENCE.

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Aims: Illicit substance use in adolescents and young adults is widespread. Marijuana and opioids are the most frequently used illicit substances, and those for which these groups most commonly seek treatment. Despite this high prevalence, little research has characterized these groups of treatment-seekers. The purpose of this secondary analysis is to characterize and compare young adults seeking treatment for opioid dependence to those seeking treatment for cannabis dependence.
Methods: We looked at baseline characteristics and patterns of drug use in 49 opioid-dependent (OD) young adults (aged 18-25) and 57 cannabis-dependent (CD) young adults seeking treatment at a university-based research clinic.
Results: Of the entire sample (N=106), 59% reported "high" use (>21 joint equivalents/wk in the CD group (CDG); >5 heroin bag equivs/wk in the OD group (ODG)); there was no significant difference between the number of high users in each group (p=0.66). The mean age of the ODG was 22.6 years (SD=1.8) vs. 22.2 years (SD=2.1) in the CDG. The ODG was 32.7% female and the CDG was 24.6% female. The distribution of race was significantly different between the groups (p<0.01). Eighty four percent of the ODG were white and 0% were black; 23% of the CDG were black and 35% were white. Mean education years in the ODG was 13.5 (SD=1.6) vs. 13.7 (SD=2.3) in the CDG. Those in the ODG had a mean baseline GAF of 60.4 (SD=8.4) vs. 64.0 in the CDG (SD=7.8) (p<0.05). The two groups did not differ significantly in terms of frequency of use (OD: 29.2 d/month SD=2.9 vs. CD: 29.1 SD=1.9). Mean age at first use of primary drug was 15.0 yrs (SD=2.2) in the CDG vs. 18.7 yrs (SD=2.4) in the ODG (p<0.01). Age at regular use was 16.9 yrs (SD=2.5) in the CDG and 19.7 (SD=2.3) in the ODG (p<0.01). The ODG was more likely to use concurrent substances (p<0.01).
Conclusions: The two groups are similar demographically with the exception of race. Younger CD patients are more likely to be using cannabis alone, and younger OD patients may be more functionally impaired and using concurrent substances.
Financial Support: NIDA

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FACTORS ASSOCIATED WITH DIFFERENTIAL USE OF MENTAL HEALTH SERVICES AMONG WOMEN OVER 8 YEARS AFTER SUBSTANCE ABUSE TREATMENT.

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Aims: Continued receipt of a threshold level of mental health services has been associated with better long-term drug treatment outcomes but the factors related to use of services, particularly among women with substance use disorders, are poorly understood. We employ the Andersen behavioral model of health services utilization to investigate individual- and treatment system-level characteristics associated with use of differential amounts of mental health services among women treated for substance abuse.
Methods: We analyzed data provided by a prospective observational study of women (n=4,447) treated for substance abuse in California during 2000-2002 for whom we acquired administrative records on mental health services utilization covering 8 years post-admission. We identified predisposing, enabling, and need characteristics associated with utilization of different amounts of mental health services, defined as none, low to moderate (>0 to <6 services per year), and high (>=6 services per year).
Results: Over 8 years, 50% of women utilized some amount of mental health services; 33% utilized a high amount (13% in only a single year, 20% in more than one year). Preliminary logistic regression analysis indicated that the likelihood of utilizing a high amount of mental health services in one or more years (relative to none/low to moderate use) was associated with several predisposing characteristics (Hispanic race/ethnicity [OR .77, p<.01], currently married [OR .69, p<.001], history of physical/sexual abuse [OR 1.32, p<.01], has child in court custody [OR 1.20, p<.05]) and enabling factors (duration of index drug treatment episode [OR 1.0, p<.01], receives psychiatric disability pension [OR 1.5, p<.05]), in addition to evaluated and perceived need for care.
Conclusions: Knowledge of the factors related to the differential use of mental health services among women treated for substance use disorders may aid efforts to optimize care for these women and the health care systems that serve them.
Financial Support: NIDA R01DA021183, P30DA016383, & K05DA017648 (PI: Hser)

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CANNABIS SMOKING MAY EXACERBATE DEPRESSION-ATTRIBUTABLE FUNCTIONAL IMPAIRMENT AMONG RECENTLY ACTIVE DEPRESSED CASES.

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Aims: Among the suspected health hazards of prolonged cannabis smoking is an increase in the occurrence of a depression syndrome. Clinically significant occupational and social impairments are known to be attributed to depression. We surmise that co-occurring cannabis problems might affect these impairment levels. The aim is to estimate this hypothesized cannabis effect on this facet of the lives of depression cases.
Methods: After nationally representative sampling and recruitment, computerized self-interviews of the U.S. National Surveys of Drug Use and Health identified depression cases with recent episodes (n=13,743). Depression-related impairment was measured using a modified Sheehan Disability Scale (SDS). Features of CP were items tapping DSM-IV criteria for cannabis use disorders. Latent variable analysis was conducted in Mplus to regress a continuous depression impairment trait on a CP trait, with covariate adjustments.
Results: One-fourth of these depression cases attributed severe to very severe functional impairments to their mood disturbances, with more pronounced impairments in relationships and social life domains. At higher levels of CP there was greater depression-related impairment (beta=0.2; 95% CI= 0.1,0.3). Findings could not be accounted for by model covariates or by depression occurring prior to cannabis onset (i.e., self-medication hypothesis).
Conclusions: Our evidence points to a more impairment-laden depression with impairments in work, home-life, and social relationships when depression co-occurs with problematic cannabis smoking. Randomized clinical trials with cannabis cessation outcomes may be required to produce more definitive evidence of this possible effect of cannabis problems on depression severity.
Financial Support: NIDA T32DA021129 (BJF); K05DA015799 (JCA).

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INCOME VARIABILITY BY RACE IN TOBACCO OUTLET DENSITY IN MARYLAND.

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Aims: Much of the research on tobacco outlet density has focused on its relationship with demographics. Studies have shown that higher concentrations of minorities and lower-income individuals correlate with greater presence of tobacco outlets. Recent work considered their interaction and concluded that income level was the strongest predictor. This study continued investigation into the relationship between income and tobacco outlet density by analyzing Maryland geopolitical areas with similar racial concentrations yet differing income levels.
Methods: Population data for census tracts were obtained from the 2010 Decennial Census. Demographic data were obtained from the 2007-2011 American Community Survey. Tobacco outlet data from 2013 were obtained from the MD Judiciary Business License database. Data were geocoded in ArcMap; spatial join tool was used to determine the number of tobacco outlets per residential census tract. Analyses contrasted tobacco outlet density in predominantly White and Black geopolitical areas.
Results: Baltimore City has a population of 620,961 (63.7% Black), a median household income of $40,100, and 7.8 (SD=7.3) tobacco outlets per census tract. By contrast, Prince George's County has a population of 863,420 (65.3% Black), a median household income of $73,447, and 3.9 (SD=3.7) outlets per tract.
Baltimore County has a population of 805,029 (64.8% White), a median household income of $65,411, and 4.0 (SD=3.5) tobacco outlets per census tract. By contrast, Montgomery County has a population of 971,777 (63.2% White), a median household income of $95,660, and 3.1 (SD=3.8) outlets per tract.
Conclusions: Preliminary results indicate a statistically significant difference in tobacco outlet density among predominantly Black (p<0.001) and White (p=0.0168) geopolitical areas stratified by income level. Further analyses will explore differences among predominantly Black and predominantly White areas with similar income level.
Financial Support: This study was supported by NIDA grant T32DA007292.

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WITHDRAWN

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METHODOLOGICAL CHALLENGES WITH MARIJUANA RESEARCH IN THE U.S.

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Aims: Marijuana is the most widely used recreational drug in the U.S. In addition, Washington and Colorado have legalized the recreational use of marijuana. In light of the widespread use and increased interest in marijuana, well-designed studies producing consistent and analyzable data are needed to evaluate marijuana's impact on the public health.

There are numerous methodological challenges when conducting marijuana research. These challenges affect the analysis and interpretation of marijuana research, and limit cross study comparisons. The challenges associated with performing marijuana research are illustrated by several aspects of the study design. First, marijuana is a plant with a highly variable chemistry and complex chemical composition. Thus, the marijuana commonly used in the U.S. may be chemically dissimilar from the marijuana used in clinical studies. Second, marijuana is usually administered through smoking, and this route of administration does not allow for the administration of consistent and reproducible doses. Third, the speed of onset and robust pharmacodynamic effects of marijuana often compromise the blinding of study subjects. In addition, the varied inclusion/exclusion criteria (e.g., drug use history) may also affect a variety of outcome measures. For example, tolerance can influence dosing, blinding, and safety measures (e.g., cognitive effects and adverse events).

Conclusions: In order for clinical studies administering marijuana to produce useable data, they should employ consistent and reproducible dosing parameters, effective blinding strategies, and standardized assessments of safety and tolerability in specific subject populations.

Financial Support: This project was supported in part by an appointment to the ORISE Research Participation Program at the Center for Drug Evaluation and Research administered by the Oak Ridge Institute for Science and Education through an agreement between the U.S. Department of Energy and CDER.

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SUBSTANCE USE PATTERNS ASSOCIATED WITH ADULT ADHD IN SUD TREATMENT-SEEKING PATIENTS: RESULTS FROM THE AQUITAINE ADDICTION COHORT STUDY.

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Aims: The co-occurrence of Substance Use Disorder (SUD) and Attention Deficit/Hyperactivity Disorder (ADHD) is highly prevalent, and ADHD often worsens SUD treatment outcomes. However, whether the addiction severity in ADHD adults originates from ADHD or from other psychiatric disorders needs to be clarified. This study aimed to ascertain the factors associated with ADHD (adult and childhood-only) among SUD patients.

Methods: Newly admitted patients to an outpatient addiction clinic were interviewed with the Addiction Severity Index (ASI) for substance use history and addiction severity, the Mini International Neuropsychiatric Interview (MINI) for DSM-IV Axis I psychiatric disorders and antisocial personality disorder, and the Conners' Adult ADHD Diagnostic Interview for DSM-IV (CAADID) for the diagnosis of ADHD (childhood and adult). We performed multivariate analyses to define the factors associated with ADHD including socio-demographic characteristics, psychiatric disorders and addiction characteristics in the models. We ran the models among ADHD vs. non-ADHD patients and then among childhood-only ADHD vs. adult ADHD.

Results: 230 patients were included (64.8 males, 37.6 y.o.). Patients with ADHD were more likely males (aOR=3.0; p=.04), they were more likely to have a borderline personality disorder (aOR= 2.9, p=.049) and to exhibit an earlier onset of SUD (ORa= 4.4, p=.002) than non-ADHD patients. Adult ADHD patients were about 5 times more likely to have a polyaddiction compared to childhood-only ADHD patients (aOR= 5.3, p= .03).

Conclusions: Our findings showed that ADHD diagnosis is associated with an early onset of SUD and that a persistent ADHD diagnosis at adulthood is associated with a more severe addiction.

Financial Support: PHRC 2006, MILDT 2010

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HSV-2 AND HIV AMONG MSM WHO USE COCAINE AND HEROIN IN NEW YORK CITY.

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Aims: Most studies of the relationship of psychoactive drug use and HIV among men who have sex with men (MSM) have recruited subjects from gay-oriented settings. This raises the question of whether results for those settings can be generalized to MSM recruited from non-gay oriented settings. Several researchers have suggested that MSM recruited from gay oriented settings are more likely to engage in high risk behavior and more likely to be HIV seropositive than MSM recruited from non-gay oriented settings.

Methods: 3091 male subjects were recruited from entrants into the Beth Israel Medical Center drug treatment programs in New York City from 2005-13. Structured interviews were administered and HIV and HSV-2 antibody testing were conducted.

Results: Subjects were predominantly African-American (48%) and Hispanic (35%). Cocaine and heroin were the most commonly used drugs; methamphetamine use was rare. 8.4% of subjects reported MSM behavior. MSM had higher HIV prevalence than non-MSM males: 41% vs. 10% among non-injecting users, 24% vs. 10% among injecting users. HIV prevalence was 52% among MSM subjects who did not report sex with women vs. 17% among MSM subjects who reported sex with women (all $p < 0.01$). In multivariable analysis of MSM subjects, being HSV-2 positive, African American and Hispanic race/ethnicity, and not reporting sex with women were independently associated with being HIV seropositive.

Conclusions: HIV was quite prevalent among these primarily cocaine and heroin using MSM recruited from drug treatment programs. Additional targeted programs are needed for racial/ethnic minority MSM heroin and cocaine users, particularly those infected with HSV-2. Such programs should be implemented at non-gay oriented settings, including drug treatment programs.

Financial Support: NIH Grant Funding: 5R01DA003574

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MATERNAL RISK-TAKING PROPENSITY AND CHILDREN'S ALCOHOL USE: A LATENT GROWTH CURVE APPROACH.

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Aims: Childhood initiation of alcohol use often results in stable and chronic patterns of abuse lasting into adulthood (Masten et al., 2008). Extant research has found that parents' own alcohol use is associated with children's use over time (e.g. Latendresse et al., 2008); however, these findings cannot disentangle whether this link is due to children's observations of parental behavior (as suggested by social learning theory), or to more stable parental factors, such as parents' risk-taking propensity (consistent with a dynamic cascade framework). The current study sought to examine the effects of parental alcohol use and risk taking propensity in predicting the trajectory of youth alcohol use over four years.
Methods: Two hundred and two African-American and European-American children (44% female, M(SD)age=13 (.83)) taking part in a larger study of the development of psychopathology completed four annual assessments of their alcohol use over the past year utilizing the Youth Risk Behavior Surveillance System. Participants' mothers also reported on their own alcohol usage over the prior year and completed a behavioral measure of risk taking, the Balloon Analogue Risk Task (BART; Lejuez et al., 2002).
Results: A latent growth modeling (LGM) approach was used to test initial levels and change in children's alcohol use over time. We first examined a univariate model of alcohol use, which indicated that use increased over development. We then added mothers' baseline BART scores and past-year alcohol use as predictors of the latent intercept and slope, controlling for child demographic factors. The model fit the data well and results suggest that only mother's BART score (unstd. beta =.06, p = .045) predicted increases in alcohol use over time.
Conclusions: Our findings suggest that parental risk-taking propensity predicted the developmental trajectory of children's alcohol use above parent's own alcohol use. Results are discussed with regard to supporting a dynamic cascade framework and implications for targeting prevention efforts.
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IMPULSIVITY AND EARLY ONSET OF ALCOHOL AND CIGARETTE USE IN ADOLESCENTS.

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Aims: According to national data (ESTUDES, 2010), Spanish adolescents start using tobacco and alcohol, on average, when they are between 13 and 14 years of age. Early use of these substances poses a high risk for adolescents' health as well as a risk factor for developing problematic use of drugs in the future.The aim of this study was to analyze the role of impulsivity to predict early use of alcohol and tobacco in a big sample of young adolescents.
Methods: A total of 1246 adolescents (mean age = 13.09 y.o.) from 19 schools in the Principality of Asturias (Northern Spain) were surveyed to assess their alcohol and tobacco use, patterns of use, and their level of impulsivity. This last construct was evaluated with a computerized version of traditional questionnaires: Barratt Impulsivity Scale 11-A (Cosi et al. 2008) and ImpSS (Impulsive Sensation Seeking Scale, Zuckerman et al., 1993); and a behavioral task (Stroop Test)
Results: Adolescents who had already experimented with alcohol showed significantly higher scores in impulsivity (p<.95) according to BIS-11-A and ImpSS, and greater execution time and number of errors in the Stroop Test (p<.05). BIS-11-A scores were also significant predictors of early binge drinking in males (o.r.: 1.06) and females (o.r.: 1.05) according to logistic regression (p<.05; CI 95%). Early smokers scored higher in the ImpSS and BIS-11-A, and committed significantly more errors in the Stroop Test (p<.05).
Conclusions: This is the first wave of a longitudinal study to determine the role played by impulsivity in early onset of alcohol and tobacco use. Results showed that in young adolescents, higher impulsivity is significantly related to early drug use and risky patterns of alcohol use. The use of a behavioral task allows for a more valid measurement of this construct and supports those results obtained through questionnaires. Impulsivity is a crucial variable to keep in mind when designing early intervention programs and prevention strategies.
Financial Support: Ministry of Health, Social Services and Equality of Spain (Ref No. MSSSI-12-20127131)

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IMPROVING OUTCOMES FOR LOW-RISK/LOW-NEED DRUG COURT CLIENTS: LIFE IN THE FAST LANE.

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Aims: Given that all drug-involved offenders do not require the same level of supervision and treatment and that a one-size fits all approach often results in lost opportunities for success and wasted resources, drug courts have begun to develop specialized tracks for individuals with different levels of criminogenic risk and clinical need. As drug courts evolve, these tracks are being tailored to further match the profiles of specific offender subgroups. This presentation describes our evaluation of an accelerated track developed for particularly low risk/low need drug court participants.
Methods: Clients in an urban misdemeanor drug court were typically assigned to one of four tracks depending on their level of risk and need. Offenders were eligible for the new accelerated track, allowing them to graduate in 8-versus 12 weeks, if they were low-risk/low-need, employed, graduated high school, and had no alcohol use issues. These clients were required to provide 8 drug-free urines and attend 8 treatment sessions. Clients would be removed from the track for failing to meet any requirement.
Results: Findings indicated that 26% (121 of 473) of clients who entered the court during the evaluation period were eligible for the accelerated track, of which 84% continued to meet criteria and were retained in the track. Time to graduation for accelerated clients was significantly reduced to 95 days, on average (compared to 137 days for low risk/low need clients not assigned to the specialized track). Importantly, 97% remained arrest-free 6 months post-graduation with the remaining 3% (n = 2) being rearrested for minor drug offenses.
Conclusions: The accelerated track produced positive outcomes for clients and significantly reduced the amount of court resources that were expended. The development and implementation of this track by the drug court team exemplifies the principles set forth by NADCP (2013) and illustrates the need for specialized programming to address the full range of drug offenders coming through the criminal justice system.
Financial Support: Funded by NIDA grant R01-DA013096.

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NON-HETEROSEXUAL IDENTITY AND SUBSTANCE USE DISORDERS: THE MEDIATING ROLE OF BORDERLINE PERSONALITY DISORDER FEATURES.

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Aims: Non-heterosexual identity (NHSI) is associated with elevated risk for substance use disorders (SUDs) and lifetime rates of victimization. Victimization is also linked to Borderline Personality Disorder (BPD), which confers increased risk for SUDs. The current study examined whether BPD features (i.e., affective instability, identity problems, negative relationships, self-harm) are elevated in NHSI individuals and mediate the relationship between sexual identity and SUDs in two epidemiological samples from Australia and the US. Gender differences were examined given research showing increased relative risk for SUDs in NHSI females compared to males.
Methods: The Australian sample included 3,484 Caucasian participants aged 21-45, 4% reporting NHSI. The US sample was derived from the NESARC and restricted to 8,369 Caucasian participants aged 21-45, 2.4% reporting NHSI. SUDs (alcohol, cannabis, nicotine) and lifetime illicit drug use were obtained from diagnostic interviews. BPD features were derived via interview in the NESARC and self-report in the Australian sample.
Results: Results revealed elevated rates on all substance variables and BPD features in NHSI females across samples, whereas NHSI males reported elevations only for illicit drug use, and two features of BPD in the US sample (i.e., affective instability and identity problems). Mediation analyses demonstrated that BPD features, particularly self-harm, as well as affective instability and negative relationships, mediated the relationship between sexual identity and SUDs but only for females.
Conclusions: Results suggest that development of BPD features may be one mechanism through which risk for SUDs is conferred in NHSI females. These findings highlight the potential utility of SUD interventions targeting emotion dysregulation, which is considered the core dysfunction in BPD.
Financial Support: NIDA (DA007313, DA23668, DA18267); NHMRC (628911)

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NEONATAL ABSTINENCE SYNDROME IN METHADONE EXPOSED INFANTS: ROLE OF GENETIC VARIABILITY.

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Aims: NAS incidence & severity in infants exposed to methadone during gestation is independent of maternal methadone dose. The incidence & severity of NAS could be in part due to genetic variability of key genetic loci related to opioid response; the interleukin-1beta (IL-1β) & mu opioid receptor (OPRM1) genes. This study aimed to investigate the impact of genetic variability in IL-1B -31 or OPRM1 A118G on NAS incidence (treatment required) & severity (dose of morphine).
Methods: This pilot study collected cheek cells from 71 methadone exposed infants; 46 required treatment. Complete genetic & morphine treatment data were obtained for a subset of 26 NAS infants.
Results: There were no difference in IL-1B or OPRM1 genotypes between infants with, & without NAS (OR (p) = 1.9 (0.21) & 0.23 (0.24), respectively). There was also no impact of genetic variability at IL-1B and OPRM1 on morphine treatment (median, mg): initial morphine dose - wild-type (WT, n=21) 0.15 & variant (Var, n=5) 0.2 (p = 0.06) & WT (n=24) 0.17 & Var (n=2) 0.22 (p=0.73), respectively; maximum morphine dose - WT (n=21) 0.3 & Var (n=5) 0.28 (p = 0.94) & WT (n=24) 0.29 & Var (n=2) 0.24 (p=0.39), respectively; & total morphine in the first month of life - WT (n=20) 33.8 &Var (n=5) 34.8 (p = 0.67) & WT (n=23) 34.8 & Var (n=2) 25.4 (p=0.38), respectively.
Conclusions: Despite genetic variability at these loci being reported to impact opioid response in adults, our study to date has not replicated these findings in infants. However, infant numbers in each genotype group were low. Therefore, the possibility remains for an association between genetic variability and NAS, leading to predictive tools to pre-determine NAS incidence & severity. Data collection for this project continues.
Financial Support: University of South Australia Division of Health Sciences

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PRIMARY CARE BUPRENORPHINE DETOXIFICATION VS. MAINTENANCE FOR PRESCRIPTION OPIOID DEPENDENCE.

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Aims: The favorable clinical characteristics and improved treatment outcomes for prescription opioid dependent (POD) patients, and modest severity of withdrawal symptoms with buprenorphine/naloxone (bup/nx), have led physicians to offer detoxification with bup/nx for POD patients. We sought to determine whether bup/nx stabilization followed by detoxification (DTX) or maintenance (MTN) leads to greater reduction in illicit opioid use and treatment completion among POD patients treated in primary care.
Methods: 113 patients were randomized to DTX (n = 57) or MTN (n = 56) in an 18-week study. DTX patients underwent bup/nx stabilization for 6 weeks, a 4-week taper, and were offered naltrexone. DTX patients with 2 consecutive weekly urines with opioids following taper were offered re-induction onto bup/nx. MTN patients received bup/nx stabilization and maintenance for the study duration. All patients were offered physician management and drug counseling for the study duration. Urine toxicologies were collected weekly. Mean proportion of opioid negative urines was evaluated with missing urines considered positive. Treatment completion was assessed at 18 weeks. Analyses and p-values were adjusted for baseline differences and an interim safety analysis.
Results: At baseline, patients randomized to MTN reported more days of opioid use in the past 30 days than those randomized to DTX (p = .01), otherwise treatment groups did not differ. Patients assigned to MTN had a greater mean proportion of opioid negative urines compared to DTX (.64 vs .50; p = .001). MTN patients achieved longer maximum consecutive weeks of opioid negative urines (6.3 vs. 3.9, p = .005). MTN patients were more likely to complete treatment (66%, n=37 vs. 10%, n=6, p < .001) and remained in treatment longer (98 days vs. 65 days, p < .001). 30% (n=16) of DTX patients required re-induction onto bup/nx.
Conclusions: MTN is more efficacious than DTX for POD patients treated with bup/nx in primary care.
Financial Support: R01DA020576

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PLAYFORWARD: A VIDEOGAME THAT INCREASES DRUG, ALCOHOL AND SEXUAL RISK KNOWLEDGE IN TEENS.

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Aims: Substance use is often initiated during adolescence. Given that most teens play videogames and that videogames can be effective health interventions, the play2PREVENT™ Lab developed a videogame, PlayForward: Elm City Stories, for overall risk reduction and HIV prevention in 11-14 year olds. We sought to determine the impact of PlayForward on drug/alcohol/sex risk-related (DAS) knowledge.
Methods: PlayForward was developed for the iPad through an iterative process that involved researchers, educators, videogame designers/developers, and community organizations. The efficacy of 6 weeks of twice-weekly PlayForward game play (2 hours per session) is being evaluated against a set of time/attention control games in a randomized controlled trial. To date we have enrolled 165 teens and conducted 6-week and 3-month follow-up assessments of DAS knowledge on 93 using a 22-item instrument. In addition, we have analyzed videogame log files generated through iPad software in 41 teens randomized to PlayForward as a measure of intervention exposure using the R statistical software package.
Results: Participants were 53% male with a mean age of 12.9 years. There were no baseline differences in DAS knowledge. At 6-week follow-up the PlayForward group had higher DAS knowledge scores (M=15.9, S.D.=4.7) than the control group (M=12.5, S.D.=4.6; p<0.001). These differences remained at the three-month follow-up (Intervention: M=15.2, S.D.=5.2; Control: M=12.3, S.D.=4.6; p=0.005). Analysis of 603,431 events in log files revealed that the number of game levels completed during game play was positively correlated with gains in knowledge measured at 6 weeks (r=0.51; p<0.001). The correlation remained at the 3-month (r=0.50; p<0.001) follow-up.
Conclusions: Playing the videogame PlayForward is associated with increased DAS knowledge in teens. Greater exposure to the PlayForward appears to promote retention of DAS knowledge.
Financial Support: Supported by R01HD062080

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BEHAVIOR PROBLEMS AMONG COCAINE-EXPOSED CHILDREN: ROLE OF PHYSIOLOGICAL REGULATION AND PARENTING.

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Aims: We hypothesized that low baseline respiratory sinus arrhythmia (BRSA) and low RSA change in response to challenge at 13 months would mediate the relation between prenatal cocaine exposure and behavior problems at 36 months. We also hypothesized that maternal negative affect at 13 months of age would moderate the relation between RSA and behavior problems.
Methods: Participants included 216 high risk mother-infant dyads participating in an ongoing longitudinal study of prenatal cocaine exposure. Baseline RSA was calculated during an initial 3-minute video. RSA change reflects the difference between baseline RSA and average RSA during an arm restraint task. Parenting behavior was assessed from video of 10 minute parent-child interaction. Child behavior problems were assessed by maternal report.
Results: Structural Equation Modeling (SEM) was utilized to test all hypotheses. The causal paths from PCE to the 13 month BRSA and RSA change variables were significant. Contrary to expectations, RSA change was unrelated to behavior problems while low baseline RSA at 13 months predicted low rather than high behavior problems. The indirect effect linking cocaine exposure to low behavior problems via low baseline RSA was statistically significant, providing support for mediation. High maternal negative affect moderated the association between baseline RSA and behavior problems.
Conclusions: The finding that low baseline RSA predicts lower rather than higher behavior problems was unexpected and may be related to unique characteristics of the current sample. Because children with high baseline RSA are believed to be more actively engaged with their surroundings, such children may be more susceptible to the negative characteristics of their caregiving environment. Consequently, high BRSA children who experience high levels of maternal negative affect within high-risk environments may be particularly likely to develop behavior problems.
Financial Support: This project was funded by the National Institute on Drug Abuse under award number R01DA013190.

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EFFECTS OF HZ-166, A NOVEL α2 AND α3 SUBUNIT-CONTAINING $GABA_A$ RECEPTOR AGONIST, ON INFLAMMATORY PAIN AND OPERANT BEHAVIOR IN MICE.

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Aims: GABAergic inhibition in the spinal dorsal horn is thought to contribute significantly to nociceptive processing. The present study assessed the anti-hyperalgesic effects of the novel 8-acetylene imidazobenzodiazepine HZ-166 which demonstrates selective efficacy at α2 and α3 subunit-containing $GABA_A$ receptors. For comparison, the effects of HZ-166 were also assessed in an assay of schedule-controlled responding.
Methods: The antihyperalgesic effects of HZ-166 were assessed in a model of inflammatory pain. Here, the yeast extract zymosan A (24 hr pretreatment; 0.06 mg/0.02 μg) was injected subcutaneously into the plantar surface of the foot-pad. Mechanical sensitivity was then assessed before and 10-320 min following HZ-166 administration. In a separate group, the response rate-decreasing effects of HZ-166 were examined in an assay of schedule controlled responding. Here, mice were trained on a fixed ratio 3 schedule of liquid food presentation. Once response rates were stable, the response rate-altering effects of HZ-166 were assessed.
Results: In the model of inflammatory pain, injection of zymosan A produced an increase in sensitivity to mechanical stimulation. HZ-166 (1.0 – 32 mg/kg, i.p.) produced dose- and time-dependent reversal of mechanical sensitivity and peak effects were observed at 80 min. When administered as an 80 min pretreatment, HZ-166 (3.2 – 32 mg/kg, i.p.) did not produce significant changes in response rates in the assay of schedule controlled responding.
Conclusions: These data provide evidence suggesting that systemic administration of a α2 and α3 subunit-containing $GABA_A$ receptor agonist produce selective antihyperalgesic effects while having minimal effects on operant responding. Together, these observations should provide a framework for studying $GABA_A$ receptor pharmacology which in turn should help guide the development of improved therapeutic agents for the treatment of pain.
Financial Support: RU Seed Funding Award (BDF) and NIH grant NS076517 (JMC)

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HEPATITIS C INFECTION AMONG HISPANICS IN CALIFORNIA.

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Aims: Hispanics in California are significantly more likely to be infected with hepatitis C (HCV) than Blacks or Other Ethnicities. Those Hispanics who have been infected have had their infection detected later, and they have been less likely to be linked to treatment. We aimed to compare HCV-infected Whites to Hispanics.
Methods: 2366 individuals were tested for antibodies to HCV from August 31, 2000 through September 22, 2013. The Risk Behavior Assessment that collects risk factor and demographic information, and informed consent using a form approved by the IRB was administered by trained interviewers.
Results: Bivariate results show that Hispanics who are HCV infected are also more likely to be infected with Hepatitis A, and are more likely to have been in methadone detoxification, and methadone maintenance. They used marijuana fewer, and illicit methadone more, days than other ethnicities infected with HCV. HCV-infected Hispanics spent significantly more time (Mean of 1000 days difference) incarcerated than other HCV-infected ethnicities. In a comparison of multivariate logistic regression models, Hispanics who were HCV infected were more likely to use crack, less likely to use powder cocaine, and less likely to be infected with Chlamydia than other HCV-infected individuals.
Conclusions: It is important to provide bilingual HCV testing linked to methadone treatment and to provide more written information that explains prevention, detection, and treatment of HCV in both Spanish and English. An important aspect of the Affordable Care Act implementation will be to link HCV-infected Hispanics into treatment.
Financial Support: The project described was supported by Award Numbers R01DA030234 from the National Institute on Drug Abuse, P20MD003942 from the National Institute of Minority Health and Health Disparities, and ID10-CSULB-008 from the California HIV Research Program.

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UNCOMFORTABLY NUMB: SUBSTANCE USE ASSOCIATED WITH ELDER MISTREATMENT.

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Aims: Elder mistreatment is a significant public health problem and is associated with substantial excess mortality. Evidence from a handful of studies suggests associations to link EM with using substance use (SU). Using a large and unparalleled administrative database of Adult Protective Services validated EM cases, this study estimates the prevalence of SU related EM and describes the types of EM most commonly associated with SU.
Methods: An exploratory descriptive analysis, of APS archived data with N= 7580 EM cases substantiated between 2004-2008 in Texas was performed. Demographics, EM type and data on alcohol, prescription drug abuse and illicit drug use were collected.
Results: Overall, SU associated EM occurred in n=465 (6.1%) of the cases. Thirty-two percent of the users were victims, 63% were caregivers, and 5% were a combination. The most common types of abuse among victims using substances were physical neglect (139), medical neglect (64), and mental health neglect (35). Among caregivers, physical neglect (158), emotional/verbal abuse (148), and physical abuse (148) were most common. Further exploratory results revealed that medical (OR = 4.2, 95% CI: 2.6-6.5), physical (OR = 13.0, 95% CI: 6.4-26.5) and mental health neglect (OR = 8.7, 95% CI: 4.2-18.1) were statistically reliably associated with victim substance use compared to caregiver use. However, when caregivers were using substances, emotional/verbal abuse (OR = 75.6, 95% CI: 18.4-310.7) and physical abuse (OR = 12.8, 95% CI: 3.9-41.6) were most likely validated.
Conclusions: This study found a comparatively high rate of SU related EM. Apparently, SU in EM substantiated cases is most commonly associated with older adults neglecting their health needs. Also, when caregivers are abusing substances emotional/verbal abuse and physical abuse are most common. Studies are needed to further understand these associations in order to determine appropriate prevention and intervention modalities in this vulnerable population.
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PREDICTORS OF THE RESPONSE TO ORAL Δ9-THC IN REGULAR CANNABIS USERS: FOCUS ON SEX DIFFERENCES.

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Aims: Limited evidence suggests that there are sex differences in endocannabinoid function and the response to exogenous cannabinoids. The purpose of this study is to further explore these differences by determining the influence of sex on the subjective, cognitive/psychomotor, and physiological effects of oral Δ9-THC in cannabis users.
Methods: Data from 30 subjects (N=18 M, 12 F) who completed Δ9-THC discrimination studies are being combined for this retrospective analysis. In each of the studies, subjects learned to discriminate between Δ9-THC and placebo. Subjects then received a range of Δ9-THC doses (0, 5, 15 and a "high" dose, either 25 or 30 mg). Responses on a subjective effects questionnaire, cognitive/psychomotor performance tasks and physiological measures were assessed. Data from individual outcomes are fit to a linear mixed model with Δ9-THC dose and sex included as predictors.
Results: Initial analyses reveal expected dose-dependent effects of Δ9-THC. Specifically, Δ9-THC increased ratings on "positive" VAS items (e.g., Good Effects, Like Drug, Take Again) and those related to intoxication (e.g., High, Stoned). Δ9-THC also impaired performance, elevated heart rate and reduced temperature. Despite comparable current cannabis use patterns in male and female subjects, sex differences emerged on physiological outcomes, and interestingly, female subjects were more likely to report negative subjective effects.
Conclusions: Ongoing post-hoc analyses will assess dose-related differences in the response to Δ9-THC as a function of sex. The influence of substance use history on Δ9-THC effects will also be determined. Retrospective analyses that combine data across multiple studies are useful for investigating factors that might impact the response to drugs but cannot typically be evaluated in individual studies having small sample sizes, and can be used to guide the design of future prospective studies to more rigorously investigate specific variables contributing to increased vulnerability to drug use.
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DETERMINATION OF COTININE IN THE URINE OF PREGNANT PATIENTS ENROLLED IN A CLINICAL TRIAL FOR THE USE OF BUPROPION SUSTAINED-RELEASE AS AN AID FOR SMOKING CESSATION.

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Aims: The use of Bupropion sustained release (SR) as an aid for smoking cessation during pregnancy is currently being evaluated in a double-blind placebo-controlled clinical trial at the department of OB&GYN. Prospective assessment of the patients smoking habits during pregnancy and postpartum is based on self-reporting of the number of cigarettes smoked per day. The self-reporting is validated by the quantitative determination of the levels of cotinine in patient's urine and the exhaled CO gas.
The aim of this work was to develop an analytical method utilizing liquid chromatography-mass spectrometry (LC-MS) for the quantification of cotinine in the urine of pregnant patients participating in the clinical trial.
Methods: Cotinine was extracted from urine samples using a liquid-liquid extraction method; N-ethylnorcotinine was used as internal standard. The samples were analyzed by LC-MS.
Results: The wide range of cotinine concentrations in urine samples required construction of two calibration curves to achieve linear regression for each range. The low limit of detection (LLOQ) for the developed method is 2.3 ng/ml and was deemed sufficient for the purpose of this investigation.
To date, 52 urine samples from 11 pregnant patients were analyzed and revealed a range of cotinine concentrations between 4.7 and 2617 ng/ml. When normalized to creatinine these concentrations ranged between 7.4 and 2896 ng/mg.
Conclusions: In summary, a new LC-MS method was developed and fully validated for quantification of cotinine in patients' urine samples. Together with the exhaled CO (ppm), the levels of cotinine in urine will validate and quantify the patients self-reporting of cigarette smoking during pregnancy.
Financial Support: This work was supported by a NIDA grant RO1DA030998 to TN and GH

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IMPACT OF PSYCHIATRIC COMORBIDITY IN ENGAGEMENT IN TREATMENT AFTER REFERRAL BY AN ADDICTION LIAISON PSYCHIATRY UNIT.

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Aims: To identify patient characteristics associated with engagement in follow-up after an admission in a General Hospital.
Methods: Follow-up study. All patients admitted for medical reasons and referred to the Addiction Liaison Psychiatry Unit were included. Demographics, substance use, dual diagnosis, medical diagnosis and administrative data were obtained. Six months after discharge, patients engagement in out-patient substance abuse treatment was evaluated.
Results: Final sample of 294 patients (77% men; age: 48+11). A total of 124 (42%) (76% men; age: 52±13) were not in addiction treatment before the admission, from those, 106 (81% men; age: 53±13) were referred to an addiction community centre; the rest of 18 patients were referred to other resources (12), or rejected treatment (4), or escaped (2).
From those referred, 53% attended at least one visit. When comparing patients that were engaged to the follow versus those that missed the appointment, patients engaged presented shorter length of stay in the hospital (11±5 vs 19±14 days, p=0.01), lived with family (51% vs 37%, p=0.003) and had less comorbid psychopathology en Axis I (29% vs 44%; p=0.012). No differences in gender, age, country of origin, main drug problem, legal background, nor in the presence of infectious comorbidity between both groups were found.
Conclusions: About 42% of patients with a SUD admitted to the general hospital due to somatic reasons have not been treated for substance use disorder. Around the 50% of patients referred attended at least to one visit in a community drug center.
Profile of patients that not attended the visit was more severe: social situation, longer admission time and higher prevalence of comorbidity.
Efforts should be done by Liaison Psychiatric teams, in order to increase the retention of those patients.
Financial Support: Founded in part by Red de TrastornosAdictivos (RD06/0001/1009)

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RACE AND ETHNICITY DIFFERENCES IN A MI-BASED BRIEF INTERVENTION DELIVERED IN AN ED SETTING.

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Aims: Evidence is accumulating that motivational interviewing (MI) has larger effects in minority populations, yet most MI trials do not have sufficient numbers of minority participants to support this finding. The aim of this study was to examine race and ethnicity effects among participants in the six-site National Drug Abuse Treatment Clinical Trials Network (CTN) Screening, Motivational Assessment, Referral and Treatment in the Emergency Department (SMART-ED) trial.
Methods: The SMART-ED study contrasted the effects of a MI based brief intervention plus booster calls (BI-B) to those of screening, assessment and referral (SAR) or minimal screening only (MSO) in patients endorsing problematic drug use during an ED visit. Drug use information was collected at baseline and for the 30-day period preceding the 3-month follow-up to determine changes in days of use of the patient-defined primary problem drug. Analyses adjusted for covariates of baseline use days, DAST score and AUDIT-C score and race or ethnicity as fixed effects and Site as a random effect. Race was categorized as Black, White or Other race. Ethnicity was categorized as Hispanic/Latino or not. We hypothesized that minority patients randomized to BI-B would have significantly fewer days of substance use at 3 months than patients in the SAR or MSO conditions.
Results: Of the 1285 randomized participants, 50% were White, 34% were Black/African American, and 24% were Hispanic. The most common primary drugs of abuse were cannabis (44%), cocaine (27%), and street opioids (17%). Neither the interaction between treatment and race nor the interaction between treatment and ethnicity were statistically significant (p=.46 and p=.62, respectively).
Conclusions: The lack of an interaction effect between treatment x ethnicity and treatment x race does not support findings of larger effects of MI in minority populations. Perhaps the assumed reasons for MI being a more successful approach with ethnic minority populations are less significant when there is not continuity in the interventionist delivering care.
Financial Support: NIDA CTN

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PERINATAL SUBSTANCE USE: A PROSPECTIVE EVALUATION OF ABSTINENCE AND RELAPSE.

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Aims: To assess abstinence and relapse rates among perinatal substance users.
Methods: We evaluated data from 164 pregnant women drawn from a randomized controlled trial comparing a psychological treatment for substance use to brief advice. Participants were eligible for abstinence or relapse to a particular substance if they met minimum criteria for use in the 6 months before pregnancy, defined as ≧5 cigarettes per day, ≧7 drinks per week or ≧3 drinks per day for alcohol, and any use of marijuana and cocaine. We examined abstinence and relapse rates for each substance separately using survival analysis. Abstinence was defined as no use in the last month of pregnancy and relapse as any use in the 24 months postpartum (PP). We used the log-rank test to assess differences between the survival curves for all substances.
Results: Of the 164 women in our sample, 85 (52%) met baseline use for cigarettes, 73 (45%) for alcohol, 99 (60%) for marijuana, and for cocaine 28 (17%). In the last month of pregnancy 29 (34%) of cigarette users, 70 (96%) of alcohol users, 77 (78%) of marijuana users and 21 (75%) of cocaine users achieved abstinence. For cigarettes, alcohol and marijuana the majority of relapses occurred in the first 3 months PP, 55%, 51% and 40% respectively. Clean cocaine users, however, relapsed at a somewhat lower rate, 29%. This slower trend was significant (p=0.0028) and continued through 24 months PP, when only 38% of cocaine users relapsed compared to 83%, 83% and 69% of cigarette, alcohol and marijuana users, respectively.
Conclusions: Pregnancy-related abstinence rates were high among alcohol, marijuana and cocaine users, but not smokers. Postpartum relapse was common for all substances. The relapse rate for cocaine use was lower than the rates for the other substances. It is unclear if this difference reflects a higher baseline threshold for relapse or a greater commitment to stay clean. These findings suggest differences in the risk of abstinence and relapse between substances used by perinatal women.
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THC-LIKE EFFECTS OF NOVEL SYNTHETIC CANNABINOIDS FOUND ON THE GRAY MARKET.

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Aims: An "arms race" has developed as cannabinoid compounds are controlled by state and federal government. Other, non-controlled compounds with similar structures are being marketed in their place. In the past, novel chemical structures reported in the scientific literature, but not exploited for laboratory or clinical uses have been synthesized and sold. Disturbingly, entirely novel compounds are being designed and synthesized solely for recreational use. These compounds have not undergone any preclinical testing before being sold. The purpose of these experiments was to determine whether some of the more recent synthetic compounds sold as marijuana substitutes have discriminative stimulus effects similar to Δ9-tetrahydrocannabinol, the pharmacologically active compound in marijuana.
Methods: The compounds JWH-210, UR-144, XLR-11, AKB-48, PB-22, 5F-PB-22 and AB-FUBINACA were tested for locomotor depressant effects in male Swiss-Webster mice and subsequently for substitution in male Sprague-Dawley rats trained to discriminate Δ9-tetrahydrocannabinol (3 mg/kg, i.p.).
Results: UR-144, XLR-11, AKB-48, and AB-FUBINACA each decreased locomotor activity for up to 90 min. PB-22 and 5F-PB-22 produced depressant effects lasting 120-150 min, whereas the effects of JWH-210 lasted nearly 5 hr. Each of the compounds fully substituted for the discriminative stimulus effects of Δ9-tetrahydrocannabinol.
Conclusions: All of the synthetic compounds produced locomotor depression and discriminative stimulus effects similar to those of Δ9-tetrahydrocannabinol, which suggests that these compounds likely share the psychoactive effects of marijuana and may also have comparable abuse liability.
Financial Support: Supported by NIH N01DA-13-8908.

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DISCRIMINATIVE AND LOCOMOTOR EFFECTS OF THREE SYNTHETIC CATHINONES.

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Aims: New synthetic cathinones are being developed and sold on the gray market as older compounds used as substitutes for illegal psychostimulants themselves become legally controlled. The purpose of these experiments was to determine whether several uncontrolled cathinone compounds, which are currently sold on the gray market, stimulate motor activity and have similar discriminative stimulus effects as the widely abused psychostimulants cocaine and methamphetamine.
Methods: Pentedrone (α-methylamino-valerophenone), alpha-PBP (alpha-pyrrolidinobutiophenone) and alpha-PVP (alpha-pyrrolidinopentiophenone) were tested for locomotor stimulant effects in male Swiss-Webster mice and subsequently for substitution in male Sprague-Dawley rats trained to discriminate cocaine (10 mg/kg, i.p.) or methamphetamine (1 mg/kg, i.p.) from saline.
Results: Pentedrone, alpha-PBP and alpha-PVP produced locomotor stimulant effects with efficacy comparable to those of cocaine or methamphetamine. Effects were apparent by 10 min after administration and lasted 3 to 5 hours. Pentedrone, alpha-PBP and alpha-PVP each produced discriminative stimulus effects comparable to those of cocaine and methamphetamine.
Conclusions: These three compounds produced behavioral effects quite similar to those of cocaine and methamphetamine and are thus likely to have similar abuse liability.
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INFLUENCE OF SEX ON GRAY MATTER VOLUME DIFFERENCES BETWEEN SMOKERS AND NONSMOKERS.

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Aims: Studies have examined the effects of chronic smoking on the brain by comparing gray matter volume (GMV) in cigarette smokers to nonsmoking controls with inconsistent results. Although the studies highlight the adverse effects of smoking on brain structure, sex differences were not examined, which may contribute to the conflicting findings. Thus, the current study examined GMV differences between smokers and non-smokers and assessed differences separately in males and females. Given the potential toxic effects of tobacco smoke on brain morphology, we expected that heavy smoking, as defined by pack years would be associated with decreased GMV.
Methods: High-resolution structural data were obtained from 82 (41 male) nicotine-dependent individuals and 85 (46 male) matched healthy controls. Statistical parametric maps were created in SPM8 to perform between-group comparisons using the GM tissue segmentation output by DARTEL. A GLM was created with group (smokers vs. controls) and sex as factors of interest and voxel-based whole-brain GMV as the dependent measure. Covariates included age and global GMV.
Results: Smokers showed reduced GMV in the thalamus and greater GMV in the putamen, parahippocampus and lingual, fusiform and precentral gyri than controls. In smokers, there were no sex differences in GMVs that met corrected thresholds. Female smokers had lower GMV than female controls in the thalamus. Male smokers had less GMV than male controls in the thalamus and cerebellum. Male smokers had greater GMV than male controls in the parahippocampus and lingual, fusiform and precentral gyri. Greater number of pack years was associated with lower GMV in the thalamus of male smokers only.
Conclusions: GMV differences were greatest in the thalamus, which has the highest density of nicotinic receptors of any brain region and thus is a prime target for morphometric anomalies that may be associated with nicotine consumption. Alternatively, and not mutually exclusive, perhaps this region is particularly susceptible to one or more of the numerous toxins in cigarette smoke.
Financial Support: NIDA

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FORMAL AND INFORMAL ORGANIZATIONAL ACTIVITIES OF PEOPLE WHO INJECT DRUGS.

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Aims: People who inject drugs (PWID) are often seen only in terms of their drug use—but they are first and foremost people. People's organizational involvements and activities may shape their thoughts and risks (Friedman et al, 2013).
Methods: 300 PWID were recruited by referral from the NYC National HIV Behavioral Surveillance study in 2012-13. Each was asked to list up to 5 types of formal and 5 types of informal groups they were involved in the last year. We tested selected associations of group membership with drug and sex behaviors by sex with χ^2.
Results: 72% took part in one or more group. The most common group involvement was with harm-reduction groups (28%). Among commonly reported formal groups were religious groups (6%), women's groups (11% of women), men's groups (6% of men), support groups (e.g., NA, AA; 14%), and groups (including support groups) at probation or parole departments (17% of men, 8% of women, $p<0.05$). 3% took part in Occupy or other demonstration groups. 10% were part of an "informal hang-out" group.
Of 29 PWID who took part in informal hang-out groups, 15 spent >20 hours a week with them. Of 83 in harm reduction groups, 12 spent >20 hours a week in their activities. Those in harm reduction groups were significantly less likely to share injection preparation equipment ($p<0.05$) or to backload ($p<0.05$), and had fewer sex partners ($p<0.05$). They tended ($p = 0.054$) to be less likely to engage in any unprotected sex. Informal hang-out group membership was positively associated with giving others a syringe that you already injected with ($p<0.05$).
Conclusions: Most PWID take part in some sort of group activities. Harm reduction groups are well-developed in New York: participation with them is reported frequently by PWID. Membership in them is associated with lower self-reported injection and, perhaps surprisingly, sexual risk behavior—suggesting that harm reduction group activities may have formed a focal point or subculture of lower risk in a risky environment.
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THE IMPACT OF HIV TESTING POLICIES AND PRACTICES ON HCV TESTING.

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Aims: Hepatitis C (HCV) is the most common blood-borne infection in the U.S. HCV recently surpassed HIV as a cause of death in the US. The advent of new HCV testing techniques and treatments presents a promising platform to addressing the HCV burden. The integration of HCV services into existing HIV services has also garnered considerable national attention as an approach to increasing the availability of HCV services. The motivation for integration includes similarities between the infections: injection drug use as the most common mode of transmission and co-infection. Advancements in HIV prevention strategies and polices further heightens the need for integration. We examined the extent to which HIV testing policies and testing practices are associated with HCV testing patterns.
Methods: The study included 353 opioid treatment programs (OTPs) from the 2005 and 2011 National Drug Abuse Treatment System Survey. We used ordered logit models to examine associations between HCV testing and State HIV regulations regarding opt-out testing and pre-test counseling and the provision of HIV testing (onsite or offsite HIV testing), controlling for program characteristics.
Results: Between 2005 and 2011, the proportion of OTPs offering HIV testing that also offered HCV testing declined from 93% to 75%. OTPs offering HIV testing were more likely to offer HCV testing. OTPs in states that do not require HIV pre-test counseling were more likely to offer HCV testing. However, treatment programs in states whose HIV regulations use opt-out consent were less likely to offer HCV testing.
Conclusions: HIV testing in treatment programs presents a viable platform for increasing HCV testing. Our findings suggest that policies such as dropping pre-test counseling may facilitate integration of HCV services into existing HIV testing programs. Strategies that address the decline in offering HCV testing in programs where HIV testing is available are crucial. The effective integration of HCV services into HIV testing programs is vital to increasing early diagnoses and initiation of HCV treatment, and reducing the HCV burden among at-risk populations.
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MOTOR DEVELOPMENT IN CHILDREN PRENATALLY EXPOSED TO METHAMPHETAMINE AND TOBACCO.

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Aims: The development of motor skills in children is essential and may affect social integration and achievement in school. Prior studies found that prenatal methamphetamine-exposure (PME) and/or prenatal tobacco-exposure (PTE) is associated with motor deficits in rodents and in children. This study further investigates sex-specific drug (PTE with or without PME) effects on motor competence in young children.
Methods: The Movement Assessment Battery for Children-2 was used to determine motor skills in three domains: Manual Dexterity (MD), Aiming and Catching (AC), and Balance (BAL). Scores of 30 children with PME (7.5±0.4 years; 16 boys; 24 PME+PTE), 21 children with PTE (7.0±0.5 years; 12 boys) and 37 unexposed controls (CON; 7.4±0.3 years; 19 boys) were compared. ANOVA was used to evaluate the effects of PME, PTE, and sex on the motor scores.
Results: On MD, PTE scored poorer than PME ($p=0.04$) and CON ($p=0.002$). On BAL, PTE and PME performed worse than CON ($p=0.04$ and $p=0.005$). Although AC did not differ between groups, group differences were found on global scores (PTE vs. CON, $p=0.005$; PME vs. CON, $p=0.05$). Girls performed better on MD than boys ($p=0.03$) but no group-by-sex interaction was found. PME girls performed poorer than CON girls ($p=0.008$), while PTE boys performed poorer than CON boys ($p=0.04$) on BAL.
Conclusions: Co-morbid PME and PTE negatively affects BAL only, while PTE affects both BAL and MD in young children. The observed sex-specific drug effects on BAL were consistent with a preclinical study that found prenatal nicotine-exposed male but not female mice had a blunted response to methamphetamine-induced locomotor stimulation. Together, our findings suggest that girls may be more vulnerable to the effects of PME+PTE while the boys are more sensitive to PTE alone.
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REAL-TIME STRESS, CRAVING AND MOOD DIFFERENCES IN POLYDRUG-USING METHADONE TREATMENT RESPONDERS AND NONRESPONDERS.

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Aims: Although stress is widely believed to influence drug use and relapse, the exact relationship between stress and drugs has been difficult to elucidate. We used an ecological momentary assessment (EMA) approach to study drug use and stress events during methadone maintenance.
Methods: For up to 16 weeks opioid-dependent volunteers enrolled in methadone maintenance used smartphones as electronic diaries (EDs) to complete 3 randomly prompted (RP) entries per day and to initiate an event-contingent (EC) entry each time they used a drug or felt more stressed than usual. Urine drug screens (3 x/wk) and EC opioid use reports were used to calculate % weeks of opioid use and identify Responders (Rs; negative for opioid use >50% of wks) and Nonresponders (NRs, negative for opioids <50% of wks). RP and EC data were then compared between the two groups using multilevel models.
Results: Rs (N=50) and NRs (N=47) had 11% and 72% opioid-positive and 31% and 53% cocaine-positive weeks, respectively. NRs had higher craving ratings for heroin (d = .61) and cocaine (d = 1.08) and lower positive mood ratings (d = 1.21) compared to Rs. There was no difference in RP stress ratings or numbers of EC stress events between Rs and NRs, though NRs gave higher ratings of ability to deal with stress in both RPs (d = .48) and ECs (d = .54). The groups reported different causes of stress. NRs reported higher rates of conflict with someone (d = .50), too much to do (d = .81) and injury or health problem (d = .68), while Rs reported higher rates of just started thinking about stressful things (d = .74) and being in unsafe surroundings (d = .48).
Conclusions: Although treatment responders and nonresponders rated level of ongoing stress and frequency of stressful events similarly, the data reveal a difference in the presentation of stress as well as differences in mood and craving. These results suggest that more work on the nature of stress in the lives of drug users is needed in order to decipher the role of stress in drug use.
Financial Support: This work was supported by the NIDA Intramural Research Program.

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NEIGHBORHOOD ENVIRONMENT AND MARIJUANA USE IN URBAN YOUNG ADULTS.

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Aims: Risk factors for marijuana use in older adolescents and young adults have focused primarily on family environment and peer affiliation. A growing body of work has examined the relationship between environmental context and young adult substance use. This study builds on previous research linking neighborhood environment to young adult marijuana use by exploring two distinct features of neighborhoods, namely the physical (e.g. broken windows) and social environment (e.g. adults watching youth).
Methods: Data were obtained from a longitudinal sample of 398 predominately African American young adults living in an urban environment. The data also included observational measures of physical and social order and disorder collected on the young adult's residential block. Exploratory structural equation modeling (ESEM) was utilized to test hypothesized relationships between two distinct features of the neighborhood environment, physical disorder and social activity, and past year young adult marijuana use.
Results: A two-factor model of neighborhood environment with good fit indices was selected (CFI=0.97, RMSEA=0.037). There was a positive and significant direct effect from neighborhood physical disorder to marijuana use (0.219, $p<0.05$) controlling for sex, race, and free and reduced meals status. The direct effect from neighborhood social environment to marijuana use was not significant, however, the direct effect of neighborhood physical environment to marijuana use in young adult was positive and significant.
Conclusions: These results converge with previous research linking vacant housing with young adult marijuana use but do not provide empirical support for the neighborhood social environment as a determinant of drug taking. Better explication of the social environment is needed to understand it's relationship to drug use.
Financial Support: NIAAA R01AA015196

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SMOKING AND CARDIAC REHABILITATION PARTICIPATION.

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Aims: In this literature review we explore the relationship between cardiac rehabilitation (CR) participation and smoking and assess the need for a CR-based intensive smoking cessation intervention.

Introduction: CR, a program of structured exercise, is standard care following a heart attack, value repair/replacement or bypass surgery. CR is the second most effective way for reducing mortality following such events with a 26% risk reduction (Heran, et al., 2011). Most effective is quitting smoking, associated with a 36% reduction (Critchley & Capewell, 2003).

Methods: A literature search was conducted in PubMed, Google Scholar, and Web of Knowledge using the terms smoking and cardiac rehabilitation. Abstracts were reviewed by two authors for inclusion. Full texts of relevant articles were searched for additional citations.

Results: Smoking behavior and CR participation have a complex relationship. Smoking increases a patient's probability of being referred to CR (Brady et al., 2013), but up to 20% of these patients who are smoking do not report it (Twardella et al., 2004). Smoking is also a predictor of not enrolling in CR (OR 0.59; Turk-Adawi, 2013) and those who drop out of CR early are twice as likely to be smokers (32% vs. 16%; Wittmer et al., 2012).

As smoking is such a strong predictor of early drop out, cessation could potentially maintain participation. Additionally, greater emphasis on cessation support may encourage smokers to enroll. However, current interventions offered in CR may not be intense enough. Those still smoking upon entering CR have continued to smoke despite numerous physician recommendations.

Conclusions: CR provides an ideal place to implement an intensive smoking cessation intervention. Patients are motivated and have regular clinical contact. In a population where continued smoking has such negative effects, and previous interventions have been ineffective, the inclusion of a high-intensity intervention appears prudent.

Financial Support: NIGMS award P20GM103644

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VA HEALTH SERVICE USE FOR HOMELESS AND LOW-INCOME VETERANS: A SPOTLIGHT ON LOS ANGELES' VA SUPPORTIVE HOUSING PROGRAM.

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Aims: Homeless Veterans have high rates of mental illness and substance use. The U.S. Department of Housing and Urban Development-VA Supportive Housing (VASH) program (a Housing First effort) is central to VA efforts to serve this population. Yet, little is known about healthcare utilization patterns associated with achieving VASH housing.

We compared VA Greater Los Angeles (VAGLA) service use among: 1) formerly homeless Veterans housed in VASH (VASH Veterans, n=1,997); 2) currently homeless Veterans (n=1,760); 3) housed, low-income Veterans not in VASH (n=21,682); and 4) housed, not low-income Veterans (n=37,020) who received care from 10/1/2010-9/30/2011.

Methods: Using administrative data, we compared the four groups' medical/surgical and mental health/addiction service use (inpatient, outpatient, and Emergency Department (ED)). We controlled for demographics, need, and primary care access in regression analyses of utilization data.

Results: VASH Veterans received more inpatient, outpatient, and ED care than currently homeless; housed, low-income; and housed, not low-income Veterans. Marked differences were seen in outpatient mental health/addiction (mean 11/7/2/2 visits/yr) and opioid maintenance clinics (mean 4/1/1/1 visits/yr). Adjusting for demographics and need, VASH Veterans and the currently homeless were more likely to have an outpatient mental health/addiction visit (AOR=10.2/6.4, p<.05, with the housed, not low-income as a reference group). Adjusting first for demographics and need (model 1), then also for primary care use (model 2), HUD-VASH Veterans had the greatest decrease in incident rates outpatient mental health/addiction from models 1 to 2, becoming similar to the currently homeless (IRR 2.4/2.0, p<0.05), compared to the housed, not low-income group.

Conclusions: Currently homeless Veterans use fewer mental health/addiction services than VASH Veterans, but both groups receive more mental health/addiction care than their housed peers. VASH may enable needed service use for homeless Veterans, through links to housing and primary care.

Financial Support: VAGLA CSHIIP

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RECEIPT OF OPIOID THERAPY GUIDELINE-CONCORDANT CARE AMONG HIV+ AND HIV- VETERANS.

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Aims: To determine whether HIV+ and HIV- patients initiating opioid therapy (OT) are equally likely to receive care concordant with American Pain Society/American Academy of Pain Medicine opioid clinical practice guidelines.

Methods: We performed a nested prospective cohort study on 17,961 patients from the Veterans Aging Cohort Study who initiated long-term OT (≥90-days) between 1999 and 2009. Unadjusted and adjusted models were used to evaluate associations between HIV status and outcomes on 12 indicators derived from national OT guidelines. We calculated summary scores (i.e., number of recommended indicators received per patient/number for which they were eligible x 100) and examined trends in the receipt of individual indicators over time.

Results: Receipt of guideline-concordant care was low for both patient groups. HIV+ patients (n= 5,677) were more likely than HIV- patients (n=12,284) to receive a primary care provider (PCP) visit within 1 month (51% vs. 31%; p<.001); PCP follow-up within 6 months (89% vs. 73%; p<.001); urine drug tests (UDTs) within 1 month (8% vs. 6%; p<.001) and 6 months (18% vs. 14%; p<.001); a bowel regimen (31% vs. 25%; p<.001); and concurrent non-opioid pain medications (50% vs. 46%; p<.001). However, HIV+ patients were less likely to receive physical rehabilitation (24% vs. 31%; p<.001) or counseling (30% vs. 33%; p<.01) and more likely to receive sedative co-prescriptions (22% vs. 18%; p<.001). Overall, patients received no more than 35% of recommended care. Over time, we observed an increase in UDTs (10% to 19%; p for trend <.001) and a decrease in sedative co-prescriptions (22% to 17%; p for trend <.001).

Conclusions: Strategies to increase the provision of OT guideline-concordant care are needed as the majority of HIV+ and HIV- patients receiving incident long-term OT did not receive recommended care and there were few clinically meaningful quality improvements over time.

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PREVALENCE OF ILLICIT DRUG USE AMONG PATIENTS OF COMMUNITY HEALTH CENTERS IN EAST LOS ANGELES AND TIJUANA.

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Aims: To estimate rates of drug use in primary care clinic patients based off screening done during the Quit Using Drugs Intervention Trial (Binational-QUIT) and to evaluate whether ASSIST screening yields sufficient numbers of risky, untreated drug users to warrant the implementation of a clinic wide physician brief intervention of the Quit Using Drugs Intervention Trial (QUIT) in Los Angeles and Tijuana.

Methods: Pre-visit screening of all adult patients who agreed to participate in the waiting rooms of 2 CHCs in East Los Angeles (LA) and 6 CHCs in Tijuana (TJ) was conducted with a self-administered version of the WHO Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) using a touchscreen Tablet PC in English and Spanish. "Risky" drug use was defined as casual, frequent, or binge use without the manifestations of dependence (ASSIST 4-26). High risk for dependence was defined by an ASSIST score of 27+.

Results: 5397 patients were found eligible for the screening during the study period (LA 2507, TJ 2890). Of those, 2282 (91%) in LA, and 2808 (97%) in Tijuana, completed the ASSIST questionnaire. Illicit drug use rates were higher in LA than TJ patients: lifetime use 45% vs. 15% and past 3 month use 19% vs. 4%. Levels of drug use based on ASSIST scores were also higher: low or no use (ASSIST 0-3) 81% vs 94%, moderate use of at least one drug (ASSIST 4-26) 16% vs 5%, and high use of at least one drug (possible dependence (ASSIST 27+) 3% vs 1%.

Conclusions: Binational-QUIT demonstrates the feasibility of integrating screening for drug use in CHCs of LA and TJ using self-administered touchscreen tablet PCs. Drug misuse rates among patients of CHCs are higher than expected from household in LA 10% and TJ 6%.

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BASELINE DEPRESSIVE SYMPTOMS AND CONTINGENCY MANAGEMENT OUTCOMES IN SMOKERS.

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Aims: Contingency Management (CM) has demonstrated its efficacy in increasing treatment retention and abstinence across most substance use disorders, including nicotine dependence. Depressive symptoms are usually associated with poorer treatment outcomes in smokers. However, no study to date has explored the influence of depressive symptoms on CM treatment outcomes. The main objective of the present study was to assess the effects of baseline depressive symptoms on CM outcomes.
Methods: The sample was made up of 90 treatment-seeking smokers. Inclusion criteria were aging 18 or older, smoke 10 or more cigarettes per day and not presenting any severe psychiatric disorders or other substance use disorder. Depressive symptomatology was assessed using BDI-II. Treatment completion and smoking abstinence were selected as main outcomes. Smoking abstinence was verified though urine specimens (cotinine) and exhaled air (carbon monoxide). Participants were randomized to two treatment conditions: Cognitive behavioral treatment, CBT (n=45), and CBT + CM (n=45). CBT was applied in 1-hour group-based sessions during six weeks. CM protocol was voucher-based with a maximum earnings of 300€. Bivariate analyses were carried out as a function of baseline depressive symptoms (BDI ≥ 14) and treatment condition.
Results: Patients with baseline depressive symptoms in the CBT condition had poorer outcomes than those without depressive symptoms. However, patients with baseline depressive symptoms in the CM condition did not have worse results than those without depressive symptoms. CM treatment effect in abstinence outcomes is bigger in those with depressive symptoms.
Conclusions: Treatment-seeking smokers with baseline depressive symptoms had significantly better outcomes when receiving CM. Depressed patients benefit even more of CM than those non-depressed. In sum, CM may have particular utility for smokers with depressive symptoms.
Financial Support: This work was supported by one grant of the Ministry of Science and Innovation (MICIIN) of the Spanish Government PSI2011-22804 and by a predoctoral Grant BP11-031 from FICYT.

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PSYCHEDELIC-FACILITATED SMOKING CESSATION: AN ONLINE SURVEY.

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Aims: Pilot laboratory results suggest psilocybin may be an efficacious adjunct to smoking cessation treatment. However, no study has examined smoking cessation after psychedelic use in naturalistic settings.
Methods: We are conducting an online survey collecting demographics, smoking history, and other data from people who self-report quitting/reducing smoking after taking a psychedelic.
Results: Among current completers (N=164), LSD (49%) and psilocybin (32%) were the drugs most commonly associated with quitting/reducing, with a mode of 2-5 lifetime uses each. Participants reported smoking a mean of 12 cigs/day for a mean of 8 yrs before the experience. 62 (38%) reported total and continuing abstinence after their experience, with 29 of the 62 (47%) reporting >1 yr abstinence, and 7 (11%) reporting >10 yrs abstinence. Another 67 of the 164 (41%) reported persisting smoking reduction, from a mode of 10-20 cigs/day before, to a mode of <1 cig/month after the experience. The remaining 35 (21%) reported temporary reduction, with 6 of the 35 (17%) reporting >1 yr reduction. Although the majority of withdrawal symptoms were rated as equal in severity to previous quit attempts, depression, irritability, anxiety, and craving were rated as "much less severe." 141 of the 164 (86%) reported no premeditated intention to quit/reduce smoking, and 159 (97%) described their experience as highly meaningful, with 97 (59%) considering it among the 10 most meaningful experiences of their lives. Participants cited changed life priorities/values (26%), strengthened belief in their ability to quit (26%), and changed future orientation (17%) as the most important effects leading to quitting/reducing. Other changes reported after psychedelic use included reduced alcohol (38%) and other drug use (23%).
Conclusions: Psychedelics may prompt temporary or prolonged smoking cessation, suggesting that careful administration in a treatment context may enhance motivation in changing addictive behaviors. Psychological and neurobiological mechanisms underlying such behavioral changes require further investigation.
Financial Support: Heffter Research Institute; NIH Grants T32DA07209, R01DA003889

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THE ROLE OF DRINKING MOTIVES AMONG TOBACCO-USING PROBLEM DRINKERS IN TERMS OF COGNITIVE-BASED SMOKING PROCESSES AND QUIT FAILURE.

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Aims: We explored drinking motives in relation to cognitive-based smoking processes and quit attempts among heavy drinking smokers. We hypothesized that drinking coping motives would be associated with smoking consequences related to negative reinforcement and negative personal outcomes, inflexibility of smoking behavior, and number of lifetime failed quit attempts; observed effects for coping motives would be unique from shared variance with other motives and incrementally evident beyond the variance accounted for by health problems, smoking rate, negative affectivity, cannabis use, and gender.
Methods: The sample included 190 human subjects who were treatment-seeking, heavy drinking daily smokers (37.89% female; Mage=30.27; SD=12.46). Participants responded to community advertisements to participate in a larger study examining the efficacy of two smoking cessation interventions. Data for this study came from the baseline assessment of this larger trial. Individuals responding to study advertisements were scheduled for an in-person, baseline assessment and during which time they provided informed consent, were interviewed, and completed an on-line survey.
Results: Incremental validity of drinking motives were examined in relation to each smoking consequences subscale, barriers to cessation, acceptance and inflexibility, and failed quit attempts using hiearchical multiple regression. Coping drinking motives significantly predicted smoking consequences related to negative reinforcement, smoking inflexibility, and number of failed quit attempts.
Conclusions: Theoretical models and clinical activities focused on smoking cessation among problem drinkers may benefit from considering the role of coping-oriented drinking motives to better understanding cognitive-based smoking processes and quit behavior.
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THERAPIST TURNOVER INTENTIONS: THE PREDICTIVE ROLE OF TRAINING SATISFACTION AND EVIDENCE-BASED TREATMENT PERCEPTIONS.

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Aims: This study examined the extent to which therapist's satisfaction with evidence-based treatment training (i.e., training satisfaction) and attitudes toward the evidence-based treatment (e.g., relative advantage, complexity, compatibility) predicted their subsequent turnover intentions. Additionally, this study examined reasons for staff turnover.
Methods: 162 therapists who were providing evidence-based treatment to adolescents as part of a national dissemination and implementation initiative were asked to complete organizational surveys at the end of the initial training workshop and at 2 and 6-months post-training workshop. Additionally, therapists who left during the course of the study were contacted by research staff and asked to complete a confidential turnover interview.
Results: Overall, 55 (36%) of therapists turned-over during the project. Of the 55 therapists who turned-over, 45 (82%) completed turnover interviews. Based on these interviews, 38 (84%) reported leaving voluntarily, while 7 (16%) reported leaving involuntarily. Out of those who stated they left voluntarily (n = 38), 21 (55%) left for job-related reasons, 10 (26%) for personal reasons, and 7 (18%) for a combination of job-related and personal reasons. Multilevel analyses revealed therapists turnover intentions at 6-months were significantly predicted by therapists training satisfaction (β = -.47, p<.01), relative advantage (β = -.60, p<.001), and compatibility (β = -.56, p<.001).
Conclusions: This study provides some of the first known evidence that therapist's satisfaction with evidence-based training and their attitudes about the evidence-based treatment can influence their decision to quit.
Financial Support: Supported by SAMHSA/CSAT (contract 270200700004C) and the National Institute on Drug Abuse (NIDA; R01-DA030462),

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INCENTIVES AND ALERTS FOR IMPROVING SUBSTANCE ABUSE TREATMENT IN WASHINGTON STATE.

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Aims: To determine the impacts on program performance and client outcomes of two interventions focused on treatment for substance use disorders: financial incentives and a client-specific alert and support system.
Methods: Treatment agencies in Washington State were randomly assigned to 4 intervention arms (separately by level of care): control, incentives only, alerts only, incentive and alerts. Changes by arm over 18 months starting10/1/2013 will be evaluated for process measures of performance (engagement in outpatient treatment and continuity of care after residential or detox treatment) and outcomes (employment and arrests). Agencies in the alerts/support intervention arm receive weekly alerts with a list of clients whose service profiles may negatively impact the program's performance and links to sources on improving treatment. Agencies in the incentives arm can earn quarterly financial incentives based on a combination of achievement of benchmark levels of performance and improvements from their agency's own performance since the baseline period (previous year).
Results: The baseline median scores for the performance measures are 73% for treatment engagement for outpatient services, and 26% for continuity into follow-up treatment after discharge for detoxification, and 38% for continuity after residential treatment. We also explore the differential impact on subpopulations (e.g., racial/ethnic minorities and rural clients). We will present information on implementing the project and preliminary results from the first six months of the intervention, through March 2014.
Conclusions: The results will support policymakers in Washington State and elsewhere as they consider incentive-based payment programs and use of electronic data to support quality improvement.
Financial Support: Grant from the National Institute on Drug Abuse (R01 DA033468).

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THC-LIKE EFFECTS OF NOVEL SYNTHETIC CANNABINOIDS FOUND ON THE GRAY MARKET.

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Aims: An "arms race" has developed as cannabinoid compounds are controlled by state and federal government. Other, non-controlled compounds with similar structures are being marketed in their place. In the past, novel chemical structures reported in the scientific literature, but not exploited for laboratory or clinical uses have been synthesized and sold. Disturbingly, entirely novel compounds are being designed and synthesized solely for recreational use. These compounds have not undergone any preclinical testing before being sold. The purpose of these experiments was to determine whether some of the more recent synthetic compounds sold as marijuana substitutes have discriminative stimulus effects similar to Δ9-tetrahydrocannabinol, the pharmacologically active compound in marijuana.
Methods: The compounds JWH-210, UR-144, XLR-11, AKB-48, PB-22, 5F-PB-22 and AB-FUBINACA were tested for locomotor depressant effects in male Swiss-Webster mice and subsequently for substitution in male Sprague-Dawley rats trained to discriminate Δ9-tetrahydrocannabinol (3 mg/kg, i.p.).
Results: UR-144, XLR-11, AKB-48, and AB-FUBINACA each decreased locomotor activity for up to 90 min. PB-22 and 5F-PB-22 produced depressant effects lasting 120-150 min, whereas the effects of JWH-210 lasted nearly 5 hr. Each of the compounds fully substituted for the discriminative stimulus effects of Δ9-tetrahydrocannabinol.
Conclusions: All of the synthetic compounds produced locomotor depression and discriminative stimulus effects similar to those of Δ9-tetrahydrocannabinol, which suggests that these compounds likely share the psychoactive effects of marijuana and may also have comparable abuse liability.
Financial Support: Supported by NIH N01DA-13-8908.

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BEHAVIORAL AND MOLECULAR FACTORS CONTRIBUTING TO BENEFICIAL EFFECTS OF ENVIRONMENTAL ENRICHMENT AND EXTINCTION TRAINING ON COCAINE RELAPSE PREVENTION.

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Aims: Environmental enrichment (EE) improves learning across species. In rats, 4hr periods of EE given 24hr before + immediately after 3 weekly cocaine-cue extinction sessions (EXT+EE) deters reacquisition of cocaine self-administration for 13 sessions. Here, we determined whether 1) EXT+EE had differential effects in rats exhibiting a sign vs. goal tracking phenotype; 2) EE produced different changes in GluA1 subunit expression than no-EE; and 3) the period of EE given 24hr before vs. immediately after was more critical for deterring relapse.
Methods: Rats self-administered cocaine under an FI-2min [FR5:S]second-order schedule (0.3 mg/kg; 1hr sessions). During EXT, cocaine was not delivered but cues were contingently presented. Reacquisition of cocaine self-administration began 1wk after the last EXTsession.EE (4hr blocks) was provided 24hr before + immediately after (n=13), 24hr before (n=7), and immediately after (n=10) each EXT session. Controls received EE 6hr after (n=10) or no-EE (n=15). For EE, 4 rats were placed together in a cage allowing for social interaction, cognitive stimulation and physical exercise.
Results: EE attenuated reacquisition to a greater degree than no-EE ($p<.01$) and reacquisition was attenuated to a greater degree in sign vs. goal trackers ($p<.03$). The largest attenuation was observed in sign-trackers receiving EE. Without EXT training, EE increased total GluA1 and/or pGluA1 in NAc and vmPFC compared to no-EE ($p<.02$). When EXT was combined with EE, expression was no longer enhanced in either region. The 24hr before and immediately after periods of EE individually deterred reacquisition for 2-4sessions compared to no-EE ($p<.05$). EE given 6hr after had no effects.
Conclusions: Combining EXT training with brief periods of EE may be useful for relapse prevention in highly cue-reactive individuals. EE produces unique changes in GluA1 neuroplasticity and is most beneficial when provided both 24hr before and immediately after EXT to deter relapse.
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JUNKIE HABITUS: BEYOND DISEASE AND MORAL DEFECT.

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Aims: Background: In the U.S., there are two main theories around opioid addiction: (1) opioid addiction is a medical disease (MD) that requires pharmacotherapy (e.g.., methadone); and (2) addiction is an illness that requires complete abstinence – even prescribed medications - (abstinence model-AM). While AM programs have comparatively large attrition rates, continued heroin among methadone patients (MPs) does occur. Inquiries on drug users' perceptions of their drug use as they relate to the MD and AM theories are scarce, and drug users' rationales for continued heroin use despite MP status remain unclear. Aims: To increase our understanding of heroin users' perceptions of their own drug use based on the MD and AM theories, and to identify rationales behind continued heroin use despite MP status.
Hypothesis: Heroin users, particularly MPs, experience their drug use along the lines of the MD theory
Methods: Research methods included field observations, snowball sampling and in-depth interviews with street heroin users, some of which were MPs, in NYC. MP enrollment guided recruitment. Interviews were recorded, transcribed and coded. Common experiences around the MD and AM models and heroin use were identified using a grounded theory approach.
Results: Four participants (2 MPs) were recruited by the researcher and these recruited 24 participants. Of 28 participants, 15 were MPs. Most were Hispanic (57%) and Caucasian (32%). Most were homeless (64%) males (86%) with High School or less (86%). The average age was 37. All were using heroin. Regardless of MP status, a common theme around drug use rationales was "weak will", resembling the AM addiction theory. Also, heroin-centered emotions, identities and minds influence heroin use. This phenomenon resembles a Junkie habitus, displaying deeply-ingrained heroin dispositions.
Conclusions: Regardless of MP status, the AM model is pervasive and a Junkie habitus influences continued heroin use. More research is needed to understand the interplay between the deeply-ingrained abstinence-based subjectivities and continued drug use despite MP status.
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CONTRIBUTIONS OF GLIAL GLUTAMATE TRANSPORT AND NMDA RECEPTORS IN NICOTINE RELAPSE.

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Aims: Addiction to nicotine produces long-lasting, stable changes in brain synaptic physiology that might contribute to the vulnerability to relapse. Cues associated with nicotine use can precipitate relapse, and using a rat model of cue-induced reinstatement of nicotine seeking, we quantified relapse-associated nucleus accumbens core (NAcore) extracellular glutamate as well as synaptic plasticity via morphological changes in dendritic spine head diameter and electrophysiological estimates of excitatory synaptic transmission (AMPA:NMDA ratio).
Methods: Rats were trained to self-administer nicotine (0.02 mg/kg/infusion). Rats were then placed in extinction, followed by reinstatement. Responding to the lever previously associated with drug was the measure of nicotine-seeking behavior.
Results: Withdrawal from nicotine caused a basal increase in diameter and ratio compared to yoked saline animals, and nicotine seeking elicited further increases within 15 min. Spine enlargement has been associated with increased synaptic strength, as well as upregulation in surface expression of GluA subunits of AMPA and GluN2B-containing NMDA receptors. We found that GluA1, GluN2A, and GluN2B were upregulated after extinction from nicotine in parallel with an increase in diameter and ratio. Additionally, a decrease in the glial glutamate transporter GLT-1 was found. When nicotine seeking was reinstated, there were parallel increases in responding and NAcore extracellular glutamate. These findings suggest that targeting glutamate transmission might inhibit cue-induced nicotine seeking. In support of this, inhibition of GluN2A with TCN-201 or GluN2B with ifenprodil, as well as upregulation of GLT-1 with N-acetylcysteine, abolished reinstated nicotine seeking.
Conclusions: These results indicate that up-regulated GluN2A, GluN2B, down-regulated GLT-1, and rapid synaptic potentiation in the accumbens contribute to cue-induced relapse to nicotine, and may be important pharmacotherapeutic avenues in reducing nicotine relapse.
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METHODS OF PRE-POST ANALYSIS IN THE PRESENCE OF MISSING DATA.

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Aims: To compare statistical analysis methods for testing randomized treatment group differences in common clinical trials designs with a single pre and post treatment measurement in the presence of missing data. Complete case (CC) analysis uses only subjects with both pre and post. Available case (AC) analysis uses all data collected. Mixed effects models and multiple imputation are two approaches to AC analysis. Baseline can be adjusted for in two ways either as part of the outcome (through a change score) or as a covariate (ANCOVA). This study aims to compare CC and AC analyses using each baseline adjustment method for data from a clinical trial of gabapentin for alcohol dependence of 40 alcohol dependent adults randomized to placebo or gabapentin.
Methods: Change score outcome (= post - pre) was tested using a t-test for CC analysis. For AC a mixed effects model was fit with pre and post as the outcome vector and time by treatment interaction was tested (analogous to a test of change scores). ANCOVA was run using CC data and using 50 imputed datasets for AC analysis. Outcomes: % of heavy drinking days (HDD), DrInC, OCDS.
Results: For HDD, both AC analysis p-values were significant ($p<5\%$), while both CC analysis p-values were marginal ($5\%<p<10\%$). For DrInC, ANCOVA p-values were not significant using CC or AC, while both change score analysis p-values were marginal, likely due to group differences at baseline. For OCDS, p-values were not significant using any method.
Conclusions: Available case methods should be used in pre-post analysis in clinical trials in order to analyze according to the intent to treat principle and so no information is lost. When choosing between adjusting for baseline as part of the outcome or as a covariate, the different interpretation of the results and what is actually of interest should be taken into consideration.
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WITHDRAWN

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ENVIRONMENTAL ENRICHMENT DECREASES NICOTINE SELF-ADMINISTRATION AND ATTENUATES NICOTINE-MEDIATED ENHANCEMENT OF OREXIN-1 RECEPTOR GENE EXPRESSION AND ERK1/2 ACTIVITY IN RAT PREFRONTAL CORTEX.

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Aims: The purpose of the current study was to determine the underlying mechanism(s) by which environmental enrichment results in neuroprotective effects in nicotine self-administration.
Methods: Rats were raised in either an enriched condition (EC) or an impoverished condition (IC) during postnatal days 21-53. Rats underwent nicotine (0.03 mg/kg/infusion, FR-1) or saline (as control) self-administration for 21 consecutive days. After the final self-administration session, we profiled mRNA expression using microarrays from the half of prefrontal cortex (PFC) of all rats. The phosphorylation levels of ERK1/2 (pERK1/2) from the other half of PFC were determined by Western Blot.
Results: Results revealed that EC rats consistently responded less for nicotine than IC rats ($F(1,10) = 16.2$, $p<0.01$). Microarray data showed that IC rats have decreased basal levels of orexin-1 receptor (OX1R) expression in PFC relative to EC rats in saline control group ($F(1,6) = 7.6$, $p<0.05$). However, OX1R expression was significantly increased in IC rats ($F(1,12) = 7.7$, $p<0.05$) but not in EC rats following nicotine self-administration. Compared to saline controls, IC rats exhibited increased pERK1 ($F(1, 10) = 5.7$, $p<0.05$) and pERK2 ($F(1, 10) = 5.9$, $p<0.05$), whereas the levels of pERK1/2 were not altered in EC rats following nicotine self-administration.
Conclusions: The attenuation of nicotine-mediated increase in prefrontal OX1R gene expression is associated with the nicotine-mediated pERK1/2 attenuation in EC rats. The alterations of OX1R and pERK1/2 may underlie the environmental enrichment-induced decrease in nicotine self-administration. Thus, these current results imply that manipulations of prefrontal ERK activity and OX1R expression may provide a highly innovative and new approach to the treatment of nicotine addiction.
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DISTINCTIVE TYPES OF EXECUTIVE DYSFUNCTION ON COCAINE DEPENDENCE AND ADHD COMPARED TO HEALTHY CONTROLS.

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Aims: Although ADHD is highly prevalent among substance users, neuropsychological studies about this association remain inconclusive. Moreover, ADHD symptoms among cocaine dependents (CD) can be hard to assess as both present impairments on executive functioning (EF). The aim of the study was to evaluate possible distinctive neuropsychological performance among ADHD, CD and controls.
Methods: 195 individuals were divided in three groups (60 controls, 72 CD, 63 ADHD). All participants were assessed using a neuropsychological battery including Digit Forward and Backwards, Trail Making, Stroop Test, Verbal Fluency, WCST, FAB and IGT. The Analysis of Covariance (ANCOVA) was used to compare the performance among the groups. All the statistical analysis were controlled for multiple comparisons (p value=.003 or less was considered significant).
Results: the three groups presented similar laterality and economic status; however, they differed on gender, age, ethnicity, years of education, IQ, and drug use. After controlling for these variables (as covariates), we observed that CD and ADHD were similar to controls on working memory, verbal fluency, abstraction reasoning, mental flexibility, and decision-making. Nevertheless, ADHD and CD showed worse performance in motor coordination (p<.001) compared to controls. ADHD patients showed poorer performance on speed processing (p=.002). On the other hand, CD patients presented more pronounced deficits on attentional span (p<.001).
Conclusions: ADHD and CD shared motor coordination deficits. ADHD patients had more impairments on speeding processing that could represent a compensatory strategy, while CD presented more pronounced alterations in verbal attention, which could be a consequence of chronic drug use.
Financial Support: Brazilian National Counsel of Technological and Scientific (CNPq) e São Paulo Research Foundation - FAPESP (2010/01272-6, 2010/15604-0/15786-1, 2011/09946-9 and 2011/19179-5) .

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FOLLOW UP OF CRACK USERS AFTER HOSPITAL DISCHARGE BASED ON PROBABILISTIC RECORD LINKAGE METHODOLOGY.

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Aims: To describe the Probabilistic Record Linkage (PRL) process to trace back one year of crack users hospitalization, as well as to follow them up after one year of their discharge to draw a profile time to relapse and the continuity of outpatient treatment.
Methods: PRL was based on two administrative databases: general outpatient and hospital information provided from the Brazilian Ministry of Health and a medical dataset from admissions of 293 crack users in the state of Rio Grande do Sul. The identifiers used were generated by a phonetic encoding function to allow for linkage among the databases.
Results: Out of 293 crack users of the main database, we found 120 exact matches in the hospitalization dataset, and 21 in the outpatient. A final exact match proportion of 7%, and 39% of possible matches were obtained, considering the linkage among all databases. The study demonstrated 88 (73%) of readmissions ranging from 1 to 9 times, and only 10 of crack users (3.4%) had access to outpatient treatment.
Conclusions: Probabilistic Record Linkage can be used to provide a broader study as well as to enrich the data quality by the integration of patient medical information. This promotes improvements of data function and decision-making based on evidence.
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MEMANTINE IMPROVES BUPRENORPHINE TREATMENT FOR OPIOID-DEPENDENT YOUNG ADULTS.

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Aims: This study evaluated the tolerability and efficacy of memantine with buprenorphine to reduce opioid abusing behavior and relapse rates after discontinuation from buprenorphine.
Methods: Eighty-seven young adult opioid dependent subjects using for 3 years predominately Caucasian, male, never married were inducted onto bup/nal 16-2 mg/day and stopped at week 9. Subjects were randomized to mem (15 or 30 mg) or placebo (PL) on week 2 continued until week 13. Initial assessments were SDS, COWS and opioid craving scale. Participants reported weekly drug use on a TLFB and had urine drug screens. The primary outcomes were change in the mean proportion of opioid use with urine toxicology, last 2-week abstinence rates and time to relapse. The main data analyses used mixed-effects regression models and survival analysis.
Results: Subjects were 79% dependent on opioids analgesics. Treatment retention during the stabilization period was above 85% until week 8 and dropped to 50% on week 10. Retention in treatment were not significantly different (log rank = 0.874; p = 0.64). Treatment with mem 30mg overall significantly reduced weekly use of opioids (TLFB + Utox) relative to placebo and mem 15mg groups, with a main effect (Z = 2.07, p = 0.03) and interaction of group by time effect (Z = -2.62, p = 0.008) while controlling for baseline differences. During the last 2-weeks, 99.3% of the mem 30mg group were abstinent compared to 82% of PL and 69% of mem 15mg groups (p<005, cohen's d =0.9). Time to relapse with LOCF showed 67 % of mem 30mg group abstinent after bup discontinuation compared to 33% of mem 15mg and 36% of placebo groups (NS).
Conclusions: Memantine 30mg significantly enhanced treatment with bup/nal in reducing opioid abusing behavior among young persons with opioid dependence and increased the abstinent rates at the end of the trial. Memantine effect on early relapse after buprenorphine discontinuation needs further evaluation.
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INTERNATIONAL RATES OF SUD AND ADHD SYMPTOMS AMONG PRISON INMATES: INDIVIDUAL DATA AND POOLED EFFECTS.

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Aims: Prison inmates have increased rates of psychiatric disorders and comorbidity. SUDs are considerably high among adults with ADHD, and both disorders often coexist in incarcerated populations. Most studies on ADHD/SUD in prison have been conducted on Europeans. A question remains on whether rates differ internationally and across diverse ethnic groups.
This study aims to contrast the prevalence of SUD and IDU associated with ADHD symptoms across international prison inmates' samples. We also tested whether ADHD symptom domains are differentially associated with SUD.
Methods: The CIDI-SUD module and the WURS, a measure of retrospective ADHD symptoms, were completed by 1,330 male inmates: 72% Latino (PR), 15% British (UK) and 13% Nordic (Sweden and Iceland). Scores for 3 symptom domains (cognitive, internalizing and externalizing) were derived through CFA. Logistic regression models tested associations between total ADHD scores, and scores for each symptom domain with lifetime alcohol and drug dependence. We conducted meta-analysis on independent sample's results to test the overall effect size of the association.
Results: Nordic, British and Latino alcohol dependence (AD) rates were 54.5%, 16.8% and 28.4%, respectively, and 79.0%, 47.5% and 50.5% for drug dependence (DD). All ADHD symptom domains were significantly associated with DD on all samples, whereas for AD there was no association among Nordic offenders. We found a significant pooled effect for lifetime IDU, but only for the internalized ADHD symptoms domain.
Conclusions: Associations between ADHD symptoms and SUD seem consistent across samples, with a few exceptions. However, rates of SUD differ substantially. We address how different international approaches to criminal justice policies for drug offenses may affect rates and outcomes, and discuss implications of our findings for treatment of SUD within the criminal justice system.
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PREVALENCE AND PREDICTORS OF DRIVING UNDER THE INFLUENCE IN SPANISH YOUNGSTERS.

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Aims: Alcohol and other substances consume is a key risk factor for vehicle accidents in young drivers. Crashes associated with consumption typically have greater severity. The goal of this study was to examine the prevalence of driving under the influence among Spanish youngsters and to examine behaviors related to driving under the influence of alcohol and other substances among Spanish youth.
Methods: Participants included 478 college students aged from 17 to 26 years (M = 19.8; SD = 1.85). A total of 310 participants had a driving license, with most having received their licenses at the age of 18 years (M = 18.41; SD = 0.90). Of the total sample, 35.6% had their own car.
Results: Alcohol was the substance most associated with driving, with 26% of participants reporting ever driving under the influence. About 84% of participants reported having ever traveled with a drunk driver, and 4.4% reported ever having had a collision while driving under the influence of alcohol. Participants perceived that more than half of their peers (56.8%; SD = 23.9) and adults (57.2%; SD = 23.94) had ever driven under the influence of alcohol. Furthermore, males engage in higher levels of alcohol and other drug use ($p < 0.01$), and perceived less risk in drunk driving (M = 2.98; SD = 0.80). Attitudes towards drunk driving positively predicted intentions to drive under the influence of alcohol ($\beta = 0.34$; $p < 0.001$) which in turn predicted drunk driving behavior ($\beta = 0.27$; $p < 0.001$). Similarly, subjective norms regarding drunk driving positively predicted intentions to drive under the influence of alcohol ($\beta = 0.08$; $p < 0.001$) which in turn predicted drunk driving behavior ($\beta = 0.27$; $p < 0.001$).
Conclusions: The results suggest the need for preventive interventions among Spanish young drivers, taking into account the importance of changing attitudes and subjective norms in order to reduce this type of behavior.
Financial Support: Ministerio de Economía y Competitividad Reference PSI2011-26819

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CHANGES IN THE PREVALENCE OF DEPRESSION AND ANXIETY DISORDERS AMONG DAILY SMOKERS IN THE UNITED STATES: 1990 TO 2001.

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Aims: The present study investigated whether the prevalence of depression and anxiety disorders has increased over time among daily smokers, as well as whether these trends differ by gender and among non-smokers.
Methods: Data were drawn from the National Comorbidity Survey (NCS; 1990) and the National Comorbidity Survey-Replication (NCS-R; 2001), representative samples of the US adult population. Logistic regression analyses were used to determine differences between depression and anxiety disorders among daily smokers in 1990 and 2001 stratified by gender and among those who were never daily smokers.
Results: Depression and anxiety disorders were significantly more common among daily smokers in 2001 compared with 1990. Increases in anxiety disorders were more prominent among females whereas the increase in depression was only statistically significant among males. The same trends were not observed among those who were not daily smokers.
Conclusions: The prevalence of depression and anxiety disorders among daily smokers appears to have increased from 1990 to 2001. Future studies are needed to determine whether these trends have continued. If so, interventions aimed at moving the prevalence lower may have limited success if depression, anxiety disorders and other mental health conditions are not considered in the development and dissemination of tobacco control programs.
Financial Support: No external support.

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CHARACTERISTICS OF BUPRENORPHINE OPIOID AGONIST TREATMENT IN A LONGITUDINAL U.S. MEDICAID POPULATION.

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Aims: In the US, opioid agonist therapy using buprenorphine (OAT-B) has the promise of increasing access to pharmacological treatment for patients with opioid use disorders (OUD). It has been unclear whether, how, and for whom the provision of OAT-B has occurred. We sought to longitudinally describe the access to OAT-B for low income or disabled individuals. We hypothesized that the availability of OAT-B provides improved access to pharmacotherapy; average maximum doses of OAT-B have increased over time; and disproportionately more minorities receive OAT-B.
Methods: We examined annual individual claims data from the Commonwealth of Pennsylvania's Medicaid program from 2007-2011 on a state and county level. For each individual per year, we identified the maximum daily dose of OAT-B prescribed, then calculated the mean maximum OAT-B dose annually.
Results: From 2007-2011, OUD-related diagnoses increased from 31,185 to 48,540 (56% increase; mean age of 35 years, 48% females, 78% whites, and 91% enrollment in managed care plans). From 2007 to 2011, the proportion OUD patients that received OAT-B more than doubled, from 2,990 (10%) to 11,620 (24%); OAT-B prescribers increased from 600 to 1,069. For the OAT-B sample with an OUD diagnosis, in 2011 (vs. 2007), mean age was 33 (31) years, 53% (50%) were female, 90% (91%) were white, and 96% (94%) enrolled in managed care plans. From 2007-2011, the mean maximum dose of OAT-B decreased from 21.1mg/day to 17.2 mg/day. In 2011, whereas enrollees in racial minority groups made up 22% of OUD patients, they accounted for only 9% of OAT-B use. The proportionate access of OAT-B among those with OUD (and mean maximum daily dose) varied by county and longitudinally within counties over time.
Conclusions: We found increased access to OAT-B pharmacotherapy for patients with OUD in a large US state, but that its use was disproportionately low among patients with OUD who were racial/ethnic minorities. Access to OAT-B and prescribing patterns vary on county levels.
Financial Support: University of Pittsburgh, Commonwealth of Pennsylvania.

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WITHDRAWN

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PLASMA BUTYRYLCHOLINESTERASE ENZYME FUNCTIONAL ACTIVITY IN COCAINE ADDICTS.

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Aims: BChE is the major cocaine-metabolizing enzyme in primates. Enhancement of BChE enzyme activity may be a treatment approach for cocaine use disorders, but little is known about naturally occurring enzyme functional activity in drug users. This study compared BChE functional activity over time in primary cocaine users, polydrug users, and non-drug-using controls.
Methods: A convenience sample of 114 primary cocaine users (mean [SD] age 34.9 [5.1] yrs, 64% male, 25.4% white, 26.5 [7.3] body mass index [BMI], 7.8 [5.9] yrs lifetime cocaine use), 72 primary cocaine + heroin users (34.4 [6.2] yrs, 86.1% male, 27.6 [5.4] BMI, 7.5 [6.2] yrs cocaine use), 43 polydrug users (34.3 [6.2] yrs, 76.7% male, 31.2 [9.4] BMI, 5.1 [5.8] yrs cocaine use), and 21 non-drug-using healthy controls (32.3 [7.3] yrs, 71.4% male, 35.4 [14.3] BMI) provided peripheral venous blood samples for up to 1 yr for later assay of BChE functional activity via the colorimetric method of Ellman.
Results: All participants had BChE functional activity within the normal range. There was no significant drug group difference in baseline BChE functional activity (2.43-2.53 [0.80-1.59] U/mL); however a significant group effect ($F=15.11$, $p<0.0001$) emerged after adjusting for BMI ($F=6.81$, $p=0.01$). Primary cocaine users had significantly lower BMI-adjusted functional activity than controls (1.57 vs. 2.70 U/mL). There was no significant change in BChE functional activity over time.
Conclusions: Plasma BChE functional activity is not significantly affected by chronic cocaine use, either by itself or combined with other drug use, remains stable for up to one year in cocaine users, and is significantly associated with BMI. These findings suggest that enhancement of BChE functional activity as a treatment approach could be applied to a broad range of cocaine users, but might be influenced by BMI.
Financial Support: Supported by the Intramural Research Program, NIDA, NIH.

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EXPANDING ACCESS TO MAT IN PUERTO RICO: ATTITUDES, PERCEPTIONS AND TRAINING NEEDS OF PHARMACISTS AND TECHNICIANS TOWARD DISPENSING BUPRENORPHINE FOR PATIENTS WITH OPIOID DEPENDENCE.

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Aims: Previous studies have found that pharmacy personnel may have negative perceptions and fears regarding opioid dependent patients and may be unwilling to stock medications for their treatment. In this study we identify knowledge, attitudes and perceptions towards dispensing buprenorphine for patients with opioid dependence in a representative sample of pharmacists and technicians in Puerto Rico. We explore if these differ by whether or not the pharmacy accepts Medicaid.
Methods: A Probabilistic sample with 118 participants from 61 pharmacies (65% response rate) responded to a self-administered questionnaire in 2011. A univariate analysis was conducted using SPSS version 17.0 to describe the attitudes, knowledge and training needs. Bivariate analysis was conducted to assess if these differed by acceptance of Medicaid.
Results: 80% agreed they would provide service to a person with opioid dependence; 90% were willing to dispense the medication. In spite of this, 48% believe that participants can carry out thefts in the pharmacy and 50% fear for their safety. Knowledge scores did not differ by Medicaid acceptance but negative attitudes towards drug users was significantly greater among pharmacies accepting Medicaid ($p<0.000$).
Conclusions: MAT expansion efforts must take into account the knowledge and attitudes of pharmacists as an important component of the system of care. Efforts to address negative attitudes towards drug users should initiate in pharmacies serving Medicaid beneficiaries.
Financial Support: Open Society Foundation and small grant from Reckitt Benckiser.

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PERSISTENT EFFECTS OF TACRINE ON REINSTATEMENT OF NON-REINFORCED RESPONDING FOR COCAINE.

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Aims: After treatment with tacrine or certain other cholinesterase inhibitors, some individual rats develop long-lasting reductions in cocaine-reinforced behavior, described as persistent attenuation (PA). This study determined whether cholinesterase inhibition also modified reinstatement of non-reinforced responding for drug, evaluated after extinction of cocaine self-administration.
Methods: Rats trained to self-administer intravenous cocaine under FR-5 (reinforcement after 5 lever-presses), and were then pretreated with either vehicle or 10 mg/kg-day of tacrine. Tacrine was administered following drug self-administration sessions, over a 21 hour period. After reacquisition of cocaine-reinforced behavior, extinction (cues absent and responding had no consequence), reinstatement was initiated by pretreatment with 0, 3.2, or 10 mg/kg of cocaine.
Results: After tacrine pretreatment, rats either promptly reacquired cocaine self-administration at levels similar to their previous baseline, or self-administered lower levels, defined as PA negative or positive animals, respectively. Following extinction, pretreatment with cocaine elicited robust and dose-related responding on active levers in either PA negative or positive rats. At the highest dose of cocaine evaluated (10 mg/kg), active lever responding was significantly lower in PA positive rats. In addition, the time interval between responses was significantly longer in these animals. Responding on inactive levers or following low-dose cocaine did not differ.
Conclusions: In addition to effects on cocaine-reinforced behavior, this study shows that cholinesterase inhibition can attenuate reinstatement produced by high-dose cocaine, decreasing levels of lever pressing and slowing the rate of responding. These effects were not observed at a lower cocaine dose that was sufficient to motivate significant active lever responding. Because responding on inactive levers was not affected, the findings do not reflect a generalized reduction in operant responding.
Financial Support: Supported by a grant to KG from the Department of Veterans Affairs.

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CYTOKINES DURING ACUTE ABSTINENCE OF CRACK COCAINE: THE ROLE OF EARLY LIFE STRESS.

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Aims: Cytokines have been implicated in the pathophysiology of cocaine dependence disorder and early life stress (ELS). Aim: To investigate Th1,Th2 and Th17 cytokines plasma levels during acute cocaine withdrawal in women reporting childhood maltreatment (CM).
Methods: This study included 50 crack cocaine dependent women with (CRACK-ELS) and 58 without (CRACK) history of ELS. A healthy control group (HC), with 25 participants, was included to provide reference values. The Childhood Trauma Questionnaire (CTQ) retrospectively assessed childhood maltreatment history of patients. Blood samples and clinical assessment (withdrawal symptoms) were analysed at day 4th, 11th and 18th of detoxification. Flow cytometry was used for TNF- α, IFN-y, IL-2, IL-4, IL-6, IL-10, IL-17 plasma levels determination.
Results: CRACK participants recovered to control TNF-a levels after 18 days of withdrawal, while CRACK-ELS showed an exaggerated increase in TNF-a ($p=0.04$). CRACK-ELS group increase IL-4 over time in contrast with the observed increased within CRACK group ($p<0.001$). It was observed a decreasing IL-6 levels in CRACK-ELS during withdrawal in contrast with increasing in CRACK participants ($p<0.001$). A marked increase in Th1 cytokines was detected in the whole sample.
Conclusions: ELS was related to an unbalance immune recovery during acute crack cocaine abstinence, showing a shift toward Th1 immunity within the balance Th1/Th2.
Financial Support: This study was supported by CNPq, FAPERGS and CAPES.

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DAILY CO-OCCURRENCES OF MARIJUANA USE, ALCOHOL USE, AND SEXUAL INTERCOURSE AMONG AT-RISK, TRUANT ADOLESCENT GIRLS.

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Aims: Adolescence is a time in development when many girls initiate risk behaviors, including substance use and sexual intercourse. Research has shown that these behaviors tend to co-occur, particularly among girls. However, little is known about whether they tend to engage in these behaviors simultaneously on a daily level. The purpose of this study was to test the hypothesis that marijuana and alcohol use would increase the odds of girls engaging in sexual intercourse on the same day.
Methods: The sample consisted of 30 truant girls between the ages of 13-18 years. A Timeline Follow-Back calendar assessment was used to collect data on marijuana use, alcohol use, and sexual intercourse over a 90-day period.
Results: Results from a series of General Estimating Equation models analyzing 2700 days demonstrated that using marijuana on a given day increased the odds of engaging in sexual intercourse, OR=2.89, 95% CI [1.95, 4.28], p<.001. Alcohol use did not change the odds of engaging in sexual intercourse on the same day; however, frequency of alcohol use did increase the odds of engaging in sexual intercourse, OR=1.12, 95% CI [1.02, 1.07], p=0.001. When all problem behaviors were included in the same model, frequent marijuana users were less likely to engage in sexual intercourse than infrequent users, OR=0.99, 95% CI [0.98, 0.9995], p=0.04.
Conclusions: This study found an important distinction between infrequent and frequent alcohol and marijuana users and their engagement in sexual intercourse. Consistent with previous findings, frequent alcohol use was related to increased rates of sexual intercourse and should be a focus of early intervention. Further, frequent female marijuana users may have less interest in engaging in sexual intercourse or have some common factor which reduces their frequency of engaging in sexual intercourse. Intervention/prevention programs should address the differential effects of frequency of marijuana and alcohol use on the odds of engaging in sexual intercourse among girls.
Financial Support: This study was supported by National Institute on Drug Abuse grant number R34DA029871.

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INCREASED WEIGHT GAIN AND SUCROSE INTAKE DURING EXTINCTION OF NICOTINE SELF-ADMINISTRATION IN ADULT MALE RATS.

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Aims: Cigarette smoking is characterized by decreased sweet food preference and consumption, which is reversed during cessation. These changes in food intake may mediate weight gain and risk for Type II Diabetes in individuals who quit smoking. Prior studies of these effects in rodents have been limited most often to use of noncontingent nicotine administration. The purpose of this research is to characterize changes in body weight and ad libitum chow and sucrose pellet intake during extinction of nicotine self-administration (NSA).
Methods: Male Holtzman rats were given ad libitum access to sucrose and chow (C+S group) or chow only (C group), on an FR1 schedule during 23 hr sessions. When baseline food intake was stable, rats were given access to nicotine on an FR1 schedule. After NSA and food intake stabilized, saline extinction was arranged for 10 days. Food intake and weight gain were calculated relative to the last 5 days of the nicotine phase.
Results: Total food intake (sucrose plus chow) increased over time in the C+S group compared to the C group ($F=8.7$; $p<0.01$). There was no difference in the rate of chow intake between the C and C+S groups; both groups showed an immediate increase in chow intake (~25%) followed by a slow, stable increase. Sucrose intake increased at a greater rate compared to chow intake in either the C group ($F=39.9$; $p<0.0001$) and C+S group ($F=11.3$; $p<0.01$). Chow intake did not differ between groups. The increase in sucrose intake resulted in greater weight gain in the C+S group compared to the C group ($F=12.5$; $p<0.01$) and a saline control group ($F=38.8$; $p<0.0001$).
Conclusions: These results are consistent with human studies suggesting that weight gain during smoking cessation is largely due to increases in sweet food intake. In addition, they suggest that animal models that fail to include foods other than chow may underestimate the effects of nicotine withdrawal on food intake and weight gain.
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DECONSTRUCTING CLOZAPINE FURTHER: TOWARD MEDICATION FOR ALCOHOL USE DISORDER IN SCHIZOPHRENIA.

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Aims: Introduction: Drug and alcohol use disorder occurs commonly in patients with schizophrenia and dramatically worsens their clinical course. While most antipsychotics do not lessen alcohol use in patients with schizophrenia, the atypical antipsychotic clozpine (CLOZ) does, although the mechanism is unknown. Since CLOZ's toxicity severely restricts its use, understanding its mechanism of action, may lead to development of new safer drugs which could limit alcohol use in this population. We hypothesize that CLOZ's ability to decrease alcohol drinking in patients with schizophrenia is contributed to by the dopamine (DA) D2 partial agonism of its primary metabolite norclozapine (NCLOZ) as well as its DA D3/D4 antagonism. This was tested by administering NCLOZ or buspirone (BUSP, DA D3/D4 antagonist) to Syrian golden hamsters- an animal model with face and predictive validity for alcohol use in schizophrenia
Methods: Methods: Hamsters were acclimated to alcohol drinking and then treated chronically with either NCLOZ (1-20 mg/kg s.c. or BUSP (1-10 mg/kg s.c.) in a 2-bottle free-choice paradigm.
Results: Results: 10 mg/kg NCLOZ significantly reduced both alcohol intake and preference, whereas the 20 mg/kg group trended toward decreased alcohol intake. 10 mg/kg BUSP also significantly reduced alcohol intake and preference.
Conclusions: Conclusions: These data suggest that CLOZ's ability to decrease alcohol drinking may depend, in part, on its partial DA D2 receptor agonism as well as DA D3/D4 receptor antagonism. Further study of the mechanism of action of CLOZ will help develop new drugs that can safely limit alcohol and substance use in patients with schizophrenia.
Financial Support: Work supported by NIAAA Grant 1R01AA018151-02

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GLOBAL IMPACT OF PRESCRIPTION OPIOID MISUSE: EUROPE AND U.S.

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Aims: Describe prescription opioid misuse reports to poison centres (PC) in Göttingen(Germany), Milan(Italy), and US, and by patients entering treatment programs (TP) for opioid addiction in Munich, Piemonte & Puglia, and US.
Methods: PC: intentional exposures reported in 2012 for buprenorphine, methadone, and oxycodone. TP: self-reports of drug use "to get high" by patients entering therapy from Jan2012–Jun2013 for buprenorphine, methadone, oxycodone, codeine, fentanyl, morphine, hydrocodone, hydromorphone, oxymorphone, and tramadol (heroin DNS).
Results: Germany: 70% of PC calls were intentional exposures and 57% suicidal intent, methadone was most frequent (46%). 48% of TP patients reported prescription opioid as their primary drug, methadone was most frequent (36%). Italy: 77% of PC calls were intentional exposures with 51% misuse and 49% suicide, methadone was most frequent (51%). 36% of TP patients reported prescription opioid as their primary drug, buprenorphine was most frequent (43%). US: 62% of PC calls were intentional exposures and 52% suicidal intent, oxycodone was most frequent (71%); 46% of TP patients reported prescription opioid as their primary drug, oxycodone was most frequent (52%).
Conclusions: Data from PC and TP in Germany, Italy, and US illustrate similar patterns of prescription opioid misuse, a sizable minority report a prescription opioid as their primary drug. Drugs typically prescribed for treatment of opioid addiction are more misused in Europe while oxycodone is the drug of choice in the US.
Financial Support: The RADARS® System is part of Denver Health and Hospital Authority, a division of the state of Colorado. It is supported by subscriptions from pharmaceutical manufacturers.

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A PRECLINICAL MODEL OF NATURAL REWARD DEVALUATION IN COCAINE ADDICTION: EFFECTS OF DOSE.

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Aims: Cocaine addiction is associated with the emergence of negative affective states (e.g., dysphoria, irritability, anhedonia) and the devaluation of natural rewards. Our lab has developed a rodent model of this condition wherein intra-oral infusions of a natural reward, saccharin, comes to predict impending but delayed cocaine availability. Following multiple saccharin-cocaine pairings rats exhibit aversive responses to saccharin infusion, as well as increased motivation to self-administer cocaine once available (Neuron,57(5):774,2008). Here, we examined if this negative affective state varies across cocaine dose.
Methods: All rats (n=20) were trained on our task in which they experienced multiple saccharin-cocaine pairings (Neuron,57(5):774,2008). Briefly, a sweet taste cue (saccharin) was intraorally delivered (45, 3.5 s infusions, every minute across 45 minutes) immediately followed by a cocaine self-administration phase (FR1 schedule, 2 hrs). Here, 3 doses of cocaine (0.167, 0.33, 0.66 mg/infusion) were used during the self-administration phase in 3 groups tested in a within-subjects design, with dose counterbalanced across groups. Orofacial movements were video-recorded on the first and last days of conditioning at the first dose, and on the last day of conditioning during the second and third doses.
Results: As expected, all rats elicited appetitive taste reactivity on the first day of saccharin-cocaine pairings before animals learned that saccharin predicted impending but delayed cocaine availability. In contrast, on the last day of taste-drug pairings, all rats elicited aversive taste reactivity during saccharin infusion consistent with our prior findings. However, this study revealed that aversive taste reactivity did not vary across cocaine dose.
Conclusions: The results suggest that the emergence of negative affect and natural reward devaluation is not related to cocaine dose during the self-administration phase in our model. Ongoing studies are examining other factors that may influence the emergence of this state, specifically, if environmental enrichment has protective effects.
Financial Support: T32 DA007244, DA014339

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STRATEGIES TO REDUCE PRESCRIPTION OPIOID ABUSE IN THE UNITED STATES: HOW HAVE THEY INFLUENCED THE EPIDEMIC?

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Aims: Background: Over recent years, strategies such as prescription monitoring programs, REMS guidelines, "pill mill" crackdowns, universal prevention, and reformulations have attempted to address the U.S. epidemic of prescription opioid abuse and overdose. Cumulative effects of these strategies on national patterns of prescription opioid use (RxO) have not been examined previously. Aims: To update typologies of RxO previously identified from a national sample of adults being assessed for substance abuse treatment need, test for trends over time in RxO typologies, and quantify changes in initiation of heroin and non-medical use of buprenorphine and other opioid compounds.
Methods: We first conducted a latent class analysis of data from 68,374 individuals reporting current RxO from January 1, 2009 to December 31, 2012 to the ASI-MV surveillance system; 6 latent variable indicators were fit to models with 2 to 6 classes. After assigning individuals to the final model's modal class (the outcome of interest), we then performed multinomial and binomial regression, to test for trends over time in a random sample of 4000 individuals for each year, stratified by U.S. census region.
Results: Confirming prior work, a 4-class model solution fit best, defined as 'use as prescribed', 'prescribed misuse', 'abuse', and 'high risk use' classes. Compared to other classes, prevalence of 'high risk use' increased over time (p<.0001). This trend persisted until Quarter 1, 2010, then stabilized. Odds of initiation of heroin increased 71% in the 'abuse' class from 2009 to 2011 and were highest in the 'high risk use' class over time (OR=9.5 vs. 'use as prescribed'). Oxycodone ER and hydrocodone misuse declined in the 'high risk use' class and non-medical use of buprenorphine increased among all classes (all p<.0001).
Conclusions: Intervention strategies cumulatively altered national patterns of prescription opioid use.
Financial Support: Supported by a grant from the CDC

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EFFECTS OF YOHIMBINE AND HYDROCORTISONE PRETREATMENT ON OPIOID SEEKING, STRESS BIOMARKERS, AND LEARNING IN HEROIN-DEPENDENT VOLUNTEERS.

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Aims: Determine whether mu-opioid seeking, stress-related biomarkers, and associative learning are altered by manipulation of noradrenergic and glucocorticoid neurotransmission in heroin-dependent individuals.
Methods: Subjects are being evaluated under buprenorphine-maintained, inpatient conditions using a 3x3 within-subject, randomized crossover, placebo-controlled, double-blind design. In each test session, oral pretreatment doses of the alpha2-adrenergic antagonist yohimbine (YOH 0, 27, 54mg) and glucocorticoid agonist hydrocortisone (CORT 0, 20, 40mg) are administered before a hydromorphone (HYD 1.5mg unit) vs. money ($2 unit) choice, progressive ratio task. Periodic measures include stress biomarkers (blood pressure, saliva cortisol and alpha-amylase), negative mood state, and hippocampal dependent (visual associative) learning measures.
Results: In interim analyses (n=6 completers of 15 planned), YOH dose dependently increases HYD breakpoint (lin. F[1,5]=6.37, p=.053), especially during CORT 40mg (lin. YOH x quadr. CORT F[1,5]=10.77, p<.03). YOH dose dependently increases systolic & diastolic BP (lin. Fs[1,5]= 41.26 and 31.50, ps<.005); POMS Anxiety (lin. F[2,8])=2.71, p=.15; and associative learning rate (lin. F[1,5]=6.11, p<.06), more so during placebo CORT (lin. YOH x quadratic CORT F[1,5]=9.31, p<.03). YOH 27mg but not 54mg, relative to placebo, tends to increase cortisol (quadr. F[1,5]= 5.00, p<.08) but not alpha-amylase. CORT dose dependently increases cortisol (lin. F[1,5]=32.20, p<.002) and decreases learning rate (lin. F[1,5]=10.42, p<.03), but is not altering other response measures.
Conclusions: YOH-potentiated opioid seeking, blood pressure, and anxiety responses are consistent with Greenwald et al. (2013); emerging effects of YOH on cortisol and learning measures further validate this paradigm and extend findings from animal studies. CORT produces a different profile of effects than YOH (e.g. suppression of learning) and may augment YOH's effect on opioid reinforcement.
Financial Support: 2 NIH R01 DA015462 and Joe Young Sr./Helene Lycacki Funds (State of Michigan) support this research.

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SUBSTANTIAL ENANTIOMER-SPECIFIC DIFFERENCES IN THE NEUROCHEMICAL AND BEHAVIORAL ACTIONS OF THE SYNTHETIC CATHINONE MEPHEDRONE.

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Aims: Synthetic cathinones are a novel group of amphetamine-derived psychostimulants gaining popularity among drug abusers in the United States and worldwide. Mephedrone is one of the most commonly abused synthetic cathinones and exists as two enantiomers, R-mephedrone (R-MEPH) and S-mephedrone (S-MEPH). To date, no investigations into any stereospecific actions of mephedrone enantiomers have been conducted. We provide the first investigation into the stereospecific neurochemical and behavioral actions of mephedrone.
Methods: Using rat brain synaptosomes, R-MEPH, S-MEPH and racemic MEPH's ability to produce dopamine and serotonin reuptake inhibition and monoamine release were examined. Locomotor activity assays was evaluated upon acute exposure to R-MEPH and S-MEPH, as well as in a repeated, intermittent drug exposure paradigm. Conditioned place preference was determined for multiple doses of R-MEPH and S-MEPH, and the involvement of the 5-HT2C receptor in the behavioral effects of S-MEPH were determined with locomotor and conditioned place preference assays.
Results: R-MEPH, S-MEPH, and racemic MEPH produced similar effects on reupatake inhibition and release of dopamine, while S-MEPH produced significantly greater reuptake inhibition and release of serotonin compared to R-MEPH and racemic MEPH. R-MEPH produced significantly greater ambulation and stereotypy compared to S-MEPH across multiple doses, and only R-MEPH produced place preference. Pretreatment with the 5-HT2C antagonist SB242084 potentiated S-MEPH locomotor activity and place preference.
Conclusions: The two enantiomers of mephedrone possess unique and stereospecific behavioral and neurochemical profiles. The orientation of the bond at the gamma carbon plays a role in the actions of MEPH both behaviorally and neurochemically, with the 5-HT2C receptor interaction being involved with R-MEPH and S-MEPH's behavior in vivo.
Financial Support: National Institute on Drug Abuse grants DA025314, DA01342, and DA032718

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DOES HEALTH STATUS INFLUENCE ATTITUDES ABOUT AND USE OF MEDICAL MARIJUANA? FINDINGS FROM A GENERAL POPULATION SURVEY IN CALIFORNIA.

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Aims: Legalization of medical marijuana (MM) has dramatically changed access to marijuana in some states. Findings will be presented from a population-based survey in California on the relationship of health status with attitudes toward and use of MM.
Methods: The California Quality of Life Survey (2012-13) is a telephone follow-back survey of a subset of individuals (n=2,267) who had participated in a statewide probability survey. The follow-back survey obtained information on health conditions, attitudes, and behaviors. Analyses examined socio-demographic characteristics and health conditions associated with attitudes toward and use of MM in the past year. All estimates were weighted to account for survey design.
Results: Overall, 27.4% of the sample disapproved of MM use and was higher among females; Asians and Hispanics; and individuals that were married/cohabitating, had lower education and SES, were foreign-born, heterosexual (vs. sexual minority), in fair/poor health, and had no illicit drug use in past year (all $p<0.05$). Less disapproval of MM use was associated with having diabetes, chronic back problems, major depression, and alcohol or drug abuse/dependence (all $p< 0.05$). An estimated 5.2% reported that they had obtained MM in the past year. Past-year use of MM was associated with younger age, unmarried status, less than college degree, U.S. birth, and illicit use of drugs (all $p<0.05$). Although there was no difference in their self-reported overall health status, MM users had higher rates of drug abuse/dependence, alcohol dependence, major depression, chronic pain, HIV/AIDS, and gynecological problems (all $p<0.05$).
Conclusions: Disapproval of MM was associated with poorer overall health status, but was less among individuals that had several health conditions commonly associated with MM use. Study findings may be used to inform policies related to MM use and interventions to reduce behavioral health problems among users.
Financial Support: NIDA grant R01DA020826

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HOOKAH USE AMONG COLLEGE STUDENTS: PREVALENCE, MENTAL HEALTH AND DRUG USE.

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Aims: Evidence indicates that hookah use is as, if not more harmful in terms of physical health consequences, than cigarette use. Yet, it seems that hookah users may underestimate the deleterious effects of hookah use, potentially due to the lack of regulation of this substance in the US. This study examines the prevalence, demographic characteristics, relation to other alcohol and substance use, and the mental health and stress levels associated with hookah use among undergraduates at a small, Northeastern university.
Methods: Data were drawn from the American Health Association- National College Health Assessment (Spring 2009; N=1799) at one large, Northeastern university. Relationships between hookah use and other drug use, mental health problems, and stress levels were examined using logistic regression analyses.
Results: 14.1% (253/1799) of undergraduates in this sample used hookah in the past month. Hookah users were more likely to be male, older, and participants of Greek life than non-hookah users. Hookah users were more likely to use other substances, including cigarettes, cannabis, alcohol, cocaine, and amphetamines, compared with those who had not used hookah. Of all the substances measured, alcohol and cigarette use were most strongly associated with hookah use. Hookah use was not significantly associated with increased mental health problem or higher stress levels.
Conclusions: Hookah users are significantly more likely to use other substances, including alcohol, cigarettes, cannabis, cocaine, and amphetamines, compared with those who have not used hookah. This is similar to cigarette smoking, yet, unlike cigarette smoking, hookah use shows no link with mental health problems or stress. Policymakers should consider regulating hookah products and hookah lounges to demystify the perception that hookah smoking is safer and less addictive than cigarette smoking.
Financial Support: None.

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MARIJUANA USE PREDICTS COGNITIVE IMPAIRMENT AND WHITE MATTER ALTERATIONS.

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Aims: As legalization of medical and recreational marijuana (MJ) continues to spread, topping headlines and ballots across the country, conversations about MJ often highlight potential benefits. Not surprisingly, national trends show the perception of risk and harm related to MJ is at an all-time low. This view persists despite investigations which highlight significant cognitive and neural alterations in MJ smokers. Given the rise in MJ use, specifically among youth, it is critical to determine if patterns of MJ use can predict impairments in cognitive functioning and white matter alterations.
Methods: Regression analyses of 44 chronic, heavy MJ smokers revealed that more smoking episodes and higher grams of MJ used per week predicted worse performance on cognitive tasks, particularly those of executive function, including the Stroop Color Word Task and the Wisconsin Card Sorting Test (WCST).
Results: Specifically, more smoking episodes and grams used per week predicted increased commission errors and lower percent accuracy on the Stroop, as well as increased losses of set on the WCST. Higher urinary cannabinoid level predicted fewer WCST categories and increased perseverative errors.
Patterns of MJ use also predicted white matter alterations, with higher amounts and more frequent use of MJ predicting increased fractional anisotropy (FA), a measure of white matter coherence. Interestingly, once divided into early (MJ use prior to age 16) and late (MJ use after age 16) onset groups, results indicated the relationship between FA and MJ use was entirely attributed to the early onset group, suggesting a differential impact of MJ based on initiation of use.
Conclusions: Findings suggest that early exposure to MJ may result in a potential failure to prune unnecessary connections during neuromaturation. These data have implications for more efficient treatment options, as strategies may be individualized based on age of onset and current patterns of MJ use.
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VALIDATION AND PERFORMANCE OF THE ALCOHOL, SMOKING, AND SUBSTANCE INVOLVEMENT SCREENING TEST IN ADOLESCENT PRIMARY CARE PATIENTS.

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Aims: The World Health Organization's Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) has strong support as a clinical screening tool and research instrument, but has only been validated with adults. This study examined the performance of the ASSIST in an adolescent sample.
Methods: Adolescents ages 12-17 (N=525) recruited from three urban community health centers completed an interview with the ASSIST, CRAFFT, and items from the Composite International Diagnostic Interview corresponding to DSM-5 substance use disorder criteria. The properties of the ASSIST for tobacco, alcohol, and cannabis were examined with respect to internal consistency, concurrent validity, discriminant validity, and diagnostic accuracy. An abbreviated version of the ASSIST (ASSIST-Lite) was evaluated for cannabis.
Results: The ASSIST had good internal consistency ($\alpha s= .68-.88$), good concurrent validity with the CRAFFT ($r= .41-.76$; p values$< .001$), and was able to discriminate between gradations of cannabis problem severity. In receiver operating characteristics analysis of optimal clinical cut-points, the ASSIST accurately identified youth with tobacco, alcohol, and cannabis use disorders (sensitivities=95%-100%; specificities=79%-93%; area under the curve [AUC]= .90-.94), but did so at minimally low cut-points (i.e., the lowest possible score with endorsement of substance use). The ASSIST-Lite performed similarly to the ASSIST in identifying cannabis use disorders (sensitivity=96%; sensitivity=88%; AUC= .92), also at a minimally low cut-point.
Conclusions: The ASSIST had favorable psychometric properties and may have utility as a research instrument with adolescents, but scoring or risk thresholds may require revision for screening in clinical settings. The ASSIST-Lite may be sufficiently informative in clinical screening for cannabis problems.
Financial Support: NIDA 3R01DA026003-03S1 (R. Schwartz, PI).

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STIGMA MANAGEMENT FOR WOMEN IN RECOVERY.

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Aims: This study examines the lives of women in substance abuse treatment by exploring the stigmas they perceive as they reintegrate into their communities
Methods: Semi-structured interviews and observations were conducted over 9 months with 34 women in treatment. Data was collected and analyzed using a grounded theory approach of comparing emergent themes to develop theoretical conceptualizations. NVivo was used for initial, and theoretical coding processes in order to analyze women's stigma and coping mechanisms.
Results: Study participants perceived stigmas from family and intimate partners based on views of the permanence of the "addict identity". Moreover, stigmas were undergirded by norms of proper womanhood violated by women's experiences with addiction, survival sex, mothering and incarceration. Additionally, the Latina and Caucasian sample population reported perceptions of stigma embedded in racialized stereotypes of proper behavior for their ethnic community. Moreover, women also perceived stigma from treatment peers also managing psychological threats. As a result study participants employed strategies to reduce stigma and preserve their burgeoning identities.
Conclusions: This study increases knowledge available to social justice researchers and advocates working with women managing stigmas. It gives insights into how stigmas shape processes of support seeking and community reintegration. Research findings can also inform programming for their families who are also managing anger, loss and stigma. This study has implications for both trauma and stigma informed initiatives that respond to the needs of women and families with complex illness-related struggles.
Financial Support: I do not have any financial support to participate in the CPDD conference

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TRAJECTORIES OF DRUG USE FREQUENCY AFTER SUBSTANCE ABUSE TREATMENT AMONG A SAMPLE OF HOMELESS YOUTH.

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Aims: The current study aimed to (1) identify classes of trajectories in the frequency of drug use during a 12-month period among homeless youth received one of three treatments, including the Community Reinforcement Approach (CRA), Motivation Enhancement Therapy (MET), and Case Management (CM); and (2) examine whether treatment modalities, gender, ethnicity, and history of physical abuse would predict the class membership.
Methods: Participants (N = 270) were recruited from a local drop-in center. Eligible youth met the criteria of homelessness as defined by the McKinney-Vento Act and abuse or dependence for Psychoactive Substance Use or Alcohol Disorder as defined by Diagnostic and Statistical Manual for Mental Disorders-IV. Youth were randomized to receive CRA (n = 93), MET (n = 86), or CM (n = 91). Follow-up assessments were conducted at 3, 6 and 12 months post-baseline.
Results: Growth mixture modeling analysis was conducted using MPlus 7 (Muthén & Muthén, 1998-2012). A three-class model fit the data the best. About half of the sample (n = 125) fell into the "fast decreasing" class, 67 youth fell into the "slow decreasing" class and 73 youth fell into the "increasing" class. Compared to those received CM, youth received CRA showed a lower likelihood of being in the "slow decreasing" class than in the "fast decreasing" class [b = -0.75, S.E. = 0.44, p = 0.085], and youth received MET showed a lower likelihood of being in the "increasing" class than in the "fast decreasing" class [b = -0.70, S.E. = 0.41, p = 0.086]. Being African American [b = 0.17, S.E. = 0.08, p < 0.05] or female [b = 0.64, S.E. = 0.34, p = 0.059] increased the likelihood of being in the "slow decreasing" class than being in the "fast decreasing" class.
Conclusions: The current findings suggest that CRA and MET may be more effective than CM since homeless youth received CRA or MET were more likely to exhibit fast reductions in the frequency of drug use during a 12-month period.
Financial Support: This research was supported by NIDA grant R01 DA13549 to the second author.

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INTEREST FOR TREATMENT WITH EXTENDED RELEASE NALTREXONE AMONG NORWEGIAN OPIATE USERS.

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Aims: Individuals struggling with opiate addiction have traditionally been offered treatment options of either abstinence or substitution treatment with long acting opioid agonists. The latter has been implemented in many western countries as opiate maintenance treatment (OMT) and has shown to reduce harms associated with illicit opioid use. Since 2010 pharmacological treatment with extended release Naltrexone for reducing mortality risk and craving has been available in US but not in Europe. Being a relatively new treatment opportunity for opioid dependent individuals, the interest for such antagonist treatment among patients has not been surveyed. The clinical potential for such treatment is therefore unknown, which may prevent decision makers in public health systems and hospitals to implement this pharmacological option.
Methods: Using a ten-item questionnaire, n= 410 opiate users in three major cities in Norway were assessed for interest in antagonist treatment with extended release Naltrexone. A majority of responders (>50%) were receiving OMT at time of responding.
Results: More than half of the subjects were interested in antagonist treatment with extended release Naltrexone (57%) and consequent participation in such a study (56%). The majority of subjects were also interested in stopping heroin use (69%) and to reduce craving for most drugs (72%)
Conclusions: Initial results indicate a significant interest among opiate users for quitting heroin use, desire for reducing craving and a rather high level of interest for antagonist treatment with extended release Naltrexone.
Financial Support: Norwegian research council.

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HEPATITIS C VIRUS INCIDENCE AMONG HIV+ MEN WHO HAVE SEX WITH MEN: THE ROLE OF NON-INJECTION DRUG USE.

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Aims: There has been a rise in hepatitis C virus (HCV) infection in HIV-positive (HIV+) men who have sex with men (MSM). HIV/HCV co-infection complicates management of HIV and HCV, and increases the risk of serious liver disease. The aim of this study was to carry out a systematic review and meta-analysis to characterize the epidemiology of sexually-transmitted HCV infection in this population.
Methods: The search encompassed EMBASE, PubMed and BIOSIS, plus proceedings of scientific conferences and footnote chasing. To be eligible, reports must be published or presented 1990-2013, and include data on HCV incidence or risk factors for infection in HIV+MSM who were not injecting drugs. Studies were assigned quality ratings based on the Newcastle-Ottawa Scale.
Results: The search retrieved 687 abstracts after duplicates were removed. After screening, there were 12 eligible studies from Europe, Australia, North America and Asia including 10 cohort and 2 case-control studies. HCV seroconversion rates ranged between 0 – 1.18/100 person-years (PYs), median 0.39/100PYs (n= 67,426 PYs). Two studies reported that sex while high on methamphetamine (AOR 28.6) and rectal trauma or bleeding (AOR=6.2) were significantly associated with HCV seroconversion. Few studies examined the role of non-injection drug use in HCV infection.
Conclusions: Evidence points to blood as the medium of sexual HCV transmission in HIV+MSM, and the role of drug use appears to be via the facilitation of mucosally-traumatic sexual practices. The shared use of implements to administer drugs intranasally has received little attention as a possible risk factor for HCV infection in this population.
Financial Support: NIH 1RO1DA034637-01A1

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COCAINE-INDUCED SUBJECTIVE EFFECTS DIFFER BETWEEN AFRICAN AMERICANS AND CAUCASIANS.

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Aims: Aims: Epidemiology studies indicate cocaine use is more prevalent among non-Hispanic African Americans (AAs) compared to non-Hispanic Caucasians (CCs). Many factors may contribute to drug use differences however evidence shows up-take and distribution of cocaine in brain is greater in AAs compared to CCs. In light of these pharmacokinetic and bioavailability differences we determined whether the cardiovascular and subjective effects of cocaine varied between AAs and CCs.

Methods: Methods: Data was obtained from non-treatment seeking cocaine-dependent AAs (N=9) and CCs (N=9) that participated in pre-randomization infusion sessions before being admitted to an ongoing clinical trial. Each participant received randomly administered cocaine (40 mg, IV) or saline over two sessions. Cardiovascular measures and subjective ratings (visual analog scales, 0-100) were assessed at baseline (-15) and at 5 min intervals over 30min.

Results: Results: Demographic measures and drug use histories did not differ between groups (p's>0.05). Analysis of cardiovascular measures indicated diastolic blood pressure was higher in AAs compared to CCs following saline ($p<0.05$) but not cocaine. There were no significant differences in subjective ratings between groups subsequent to saline administration. Following administration of cocaine, however, AA's subjective ratings for 'HIGH' (p=0.012) and 'GOOD DRUG EFFECT' (p=0.024) were significantly greater compared to CCs over time. AAs ratings for other positive subjective effects also tended to be greater ('ANY DRUG EFFECT', p=0.083; 'LIKE DRUG', p=0.069).

Conclusions: Conclusions: Results from this pilot study suggest cocaine elicits greater subjective effects in AAs compared to CCs, which may contribute to increased prevalence of cocaine use among this group.

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ACETAZOLAMIDE, A NEW ADHERENCE MARKER FOR CLINICAL TRIALS?

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Aims: Clinical trials to evaluate a medication assume adherence to the medication dosing instructions. Adherence failures invalidate the premise and if not detected, may result in inappropriate cessation of medication development. The current "gold" standard adherence monitor employs riboflavin compounded with the medication and monitors riboflavin excretion in urine. Unfortunately, riboflavin is rapidly excreted and exhibits a high and variable physiological baseline due to dietary influx. This study evaluates the use of sub-therapeutic levels of acetazolamide (ACZ) as an improved adherence marker compatible with a once-daily medication-dosing regimen.

Methods: The absorption, blood distribution and elimination in the urine (ADE) of 15 mg/day (p.o) ACZ was examined in 10 human volunteers. The effect of an ACZ marker on the ADE of a model study medication (oxycodone (30mg/day p.o.,OXY) was also evaluated in the same subjects. Plasma, urine and whole blood samples were analyzed by liquid chromatography with mass spectrometry.

Results: ACZ pharmacokinetics (PK) showed a plasma Cmax of 1489 ng/ml (SD, 748) and a Tmax of 1h (SD, 0.4). The elimination half-life was best fit by a two-compartment model with an alpha half-life (T1/2) of 0.8h (SD, 0.5) and a beta T1/2 of 11h (SD,1.6). Inter-subject variability in AUC was very low (CV, 0.15) due to beta T1/2 predominance. Urine excretion rates (ERs) at steady state also showed low variability (CV, 0.18), ERs for 0-9h post dose were always higher than mean trough level and following a missed dose 0-9h ERs were always lower than mean trough level.

ACZ PK T1/2 was unaffected by OXY (P>0.05) and OXY pharmacodynamics were unaltered by ACZ. OXY PK data will be shown, as will ACZ ERs, followed for 1 week after final dose.

Conclusions: ACZ AUC and ER show low variability and little interaction with the model medication, consistent with a viable adherence marker. The long beta T1/2 and low ER variation may provide for extended "time since last dose" evaluation.

Financial Support: R01DA016718-08S1 (SLW), UL1RR033173 (UK CTSA)

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CIGARETTE SMOKING AND OTHER BEHAVIORAL RISK FACTORS RELATED TO UNINTENDED PREGNANCY.

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Aims: Half of all pregnancies in the US are unintended, carrying increased health risks for both mothers and infants. In addition, because the pregnancy was not planned, a woman may compound adverse outcomes by continuing to engage in unhealthy behaviors like cigarette smoking. Identifying behaviors that moderate the risk of unintended pregnancy could facilitate development of interventions to mitigate these outcomes. Delay discounting is known to be associated with 1) smoking and 2) sexual behaviors that increase the risk of unintended pregnancy. The present study used a crowdsourcing technique to determine 1) the prevalence of unintended pregnancy among smokers and 2) contributions of risky sexual behaviors and delay discounting to unintended pregnancy.

Methods: Participants were 280 women aged 18-44 years recruited via Amazon Mechanical Turk over 3 weeks. Participants completed an online survey of demographics, smoking status, reproductive history, sexual behavior, and a delay discounting task.

Results: Smokers (n=52) averaged nearly 3 times as many unintended pregnancies as non-smokers (n=228; 1.4 vs. 0.5, $p < .001$), and 4 times as many fetal losses (0.4 vs. 0.1, $p < .05$). In multivariate analyses, smoking, unemployment, number of recent male partners, and low frequency of condom use were significant predictors of unintended pregnancy. Delay discounting was significantly correlated with number of male partners and frequency of intercourse (ps < .05) in univariate analyses, but did not predict unintended pregnancy in multivariate analyses.

Conclusions: These results suggest that cigarette smoking is strongly associated with unintended pregnancy and negative pregnancy outcomes, and highlight the importance of developing interventions to decrease smoking and risky sexual behavior among women of reproductive age. More research is needed to better understand the role of delay discounting in unintended pregnancy.

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BUPRENORPHINE DISSEMINATION IN THE PUBLIC SECTOR: SOCIAL NETWORK ANALYSIS AND INSTITUTIONAL CONSTRAINTS OF PRESCRIBERS IN NEW YORK CITY.

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Aims: Aims: 1) Characterize the social networks of public sector buprenorphine providers 2) Identify features of public institutions influencing buprenorphine provision

Methods: Methods: Face to face semi-structured interviews with 49 New York City public sector buprenorphine providers 8-24 weeks after Hurricane Sandy using respondent driven sampling initiated with prescriber lists from Medicaid, SAMHSA, and public hospitals. A social network analysis and network graph was completed based on who introduced providers to buprenorphine, who they turned to for help with everyday buprenorphine problems and during Hurricane Sandy. Interview transcripts were analyzed iteratively with multiple coders and checks of inter-coder reliability.

Results: Findings: Social networks of providers were sparse and disconnected. Many had no colleagues to turn to for help with buprenorphine. A large component of their networks was centered on one institution. Prescribers adopted buprenorphine to address co-occurring disorders, reduce relapse, and because buprenorphine is less stigmatizing than methadone. Common buprenorphine problems were prior authorization, shortage of mental health resources, and diversion or misuse. Assumptions of patient non-compliance, lack of mental health services, licensing requirements, time consuming insurance authorization, diversion and need for monitoring discouraged buprenorphine adoption.

Conclusions: Discussion: Networks of prescribers need strengthening to enhance skills, resources, and cross coverage. This may also increase prescribers; new prescribers are recruited by networks, and may be attracted by colleagual support. However some disincentives to buprenorphine provision, such as insurance authorization and lack of mental health resources, require policy interventions.

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DEPENDENCE ON AMPHETAMINES INCREASES PARKINSON'S DISEASE: EFFECT OF GENDER.

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Aims: Exposure of rats to high doses of amphetamines compromises nigrostriatal dopamine systems in a manner that resembles Parkinson's disease (PD). Thus, we determined if a history of amphetamine/methamphetamine (AMPH/METH) dependence in humans was related to a higher incidence of PD later in life.
Methods: We conducted a retrospective cohort study of individuals born after 1939 who were at least 30 years of age at their most recent follow-up. Findings came from the Utah Population Data Base (UPDB) linked with statewide hospital inpatient discharge data and medical records of 26 hospitals and 195 community/physician clinics associated with the University of Utah and Intermountain Health Care systems from 1996-2011: these data accounted for 85% of all patient visits in the state of Utah during this same time period.
Results: Using ICD-9 codes we identified 16,879 individuals (9,326 men and 7,553 women) who were diagnosed with a history of AMPH/METH dependence-related disorders: 162 of these patients (87 men and 75 women) had a subsequent diagnosis of PD or prescribed Carbidopa-levodopa. Compared to matched population controls with no history of drug or alcohol abuse, we estimated the increased PD risk associated with AMPH/METH dependence to be 4.5-fold overall (95% CI 3.7, 5.6; p<0.0001), and appeared to be somewhat higher in women than men. We found no increase in PD risk in those patients who had histories of cocaine dependence only.
Conclusions: These data confirm a previous report in a California cohort (Callaghan, R. et al. Mov. Disord. 25 [2010] 2333-2339): in addition, our findings suggest that in some populations with AMPH/METH dependence histories, particularly females, the risk may be even greater than previously predicted. For comparison, we also found that a history of cocaine dependence alone was not linked to an increased expression of PD.
Financial Support: Financial Support: NIDA R01s DA031883 DA019447 and P01 DA013367 and Huntsman Cancer Foundation.

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DEVELOPMENT OF ERROR PROCESSING IN CHILDREN OF ALCOHOLICS.

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Aims: Error detection is important for adaptive behavior adjustment, and error processing deficits can contribute to impulsive behavior. Difficulty with impulse control is heightened in children of alcoholics and is a risk factor for later substance problems. This study aims to identify neural differences in error detection across development between children of alcoholics and healthy controls.
Methods: Longitudinal fMRI was conducted in offspring from alcoholic (COA; n=43) and control (nonCOA; n=30) families starting at ages 7-12yrs. Participants performed a go/no-go task during fMRI at 1- to 2-yr intervals, covering the age range of 7-17yrs. Inhibitory failures to no-go stimuli (false alarms) were recorded. Voxel-by-voxel analysis was conducted in SPM8 using a multiple regression model, designed to represent mixed linear effects and identify age-related changes between groups.
Results: False alarm rates significantly decreased across age in both groups however, significant age-related differences were found between groups in right anterior cingulate, right caudate, and left lingual gyrus during false alarms. In the cingulate and caudate, nonCOAs showed a significant increase in activation with age, consistent with normal development, while little to no change was visible in the COAs. The COAs did, however, display a significant increase in activation across age in the left lingual gyrus. Activation in this region was significantly associated with false alarm rate in the COAs, where increased activation was related to fewer false alarms.
Conclusions: These results reveal that error detection in COAs is inconsistent with that of normal development, and compensatory mechanisms (i.e. lingual gyrus activation) may allow these individuals to adapt their behavior appropriately and perform similarly to their peers. Overall, this disparate pattern of activation likely reflects an overall weakness in cognitive control circuitry, which could represent a risk factor for substance use disorders later in life.
Financial Support: This work was supported by NIH grants R01 DA027261, R37 AA07065, and T32-DA007267-19.

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RISK AND PROTECTIVE FACTORS FOR HEROIN INITIATION AND RE-INITIATION AMONG RURAL PRESCRIPTION OPIOID USERS.

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Aims: To estimate heroin initiation rate and determine risk and protective factors for heroin initiation and re-initiation among rural drug users.
Methods: Data were collected from a longitudinal cohort of 503 prescription opioid users in rural Appalachia between 2008 and 2013. Individuals at risk for initiating or re-initiating heroin use were examined at each 6-month interval for 30 months using discrete time survival analysis. Logistic regression was used to estimate models for hazard of heroin initiation in discrete time. Estimates were weighted to reflect the respondent-driven-sampling design.
Results: There were no significant differences in heroin initiation over time. Significant protective factors were older age (OR = 0.95, CI95: 0.9130 – 0.9943), more years of education (OR = 0.86, CI95: 0.7691 – 0.9569), and higher percent income from legal sources (10% increments; OR = 0.87, CI95: 0.7977 – 0.9530). Significant risk factors included number of days using Oxycontin (OR = 1.0377, CI95: 1.0102 – 1.0660), cocaine (OR = 1.13, CI95: 1.0316 – 1.2423), and methamphetamine (OR = 1.17 CI95: 1.0845 – 1.2655) in the prior month. Significant risk factors for heroin re-initiation included having a greater number of dependents (OR = 1.47, CI95: 1.004 – 2.149), self-perceived poor health (OR = 6.56, CI95: 1.467 – 29.36), and a greater number of days using cocaine (OR = 1.30, CI95: 1.047 – 1.615) in the prior month. Older age was protective (OR = 0.8393, CI95: 0.7094 – 0.9929), and risk was virtually eliminated for individuals who either had private health insurance (OR = 3.29e-6, CI95: 3.88e-7 – 2.78e-5) or were incarcerated all of the prior month (OR = 3.29e-6, CI95: 3.88e-7 – 2.78e-5).
Conclusions: Risk and protective factors were largely distinct for new heroin initiates versus those re-initiating heroin use in this sample of predominantly prescription opioid users. Preventative measures should treat these two phenomena separately, taking into account the substantive predictors of risk in each subpopulation.
Financial Support: NIH R01DA024598 and R01DA033862

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DO SOCIAL SUPPORT AND NEGATIVE EMOTIONS CONDITION THE EFFECT OF CHILD CUSTODY LOSS ON DRUG USE?

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Aims: Women of color are disproportionately involved in the Child Welfare system (CWS). Illicit drug use (ILDU) is often a precursor to losing child custody, and research shows ILDU often increases after custody loss. This study examines if social support and negative emotions condition the relationship between custody loss and increased ILDU.
Methods: Two types of custody loss are examined: official (CWS is involved) and unofficial (child living apart from mom but courts not involved). Using data on 339 African American women, longitudinal random-coefficient and -intercept models analyzed social support as a moderator and negative emotions as a mediator of the relationship between each type of custody loss and increased ILDU in the six months after.
Results: For unofficial loss, social support, but not negative emotions, condition its effect on ILDU (p<.05). For official loss, negative emotions do not mediate, but moderate, its effect on ILDU (p<.05), while social support is not significant. Thus, unofficial loss predicts increased ILDU, but only for mothers with little social support, while official loss predicts increased ILDU only for women with a high degree of negative emotions surrounding the loss.
Conclusions: Findings suggest the mechanisms that protect against increased ILDU after custody loss vary based on the nature of the loss. So while social support is important for women who unofficially lose custody, negative emotions matter for women who lose official custody. Given the overrepresentation of African American women with substance use problems in the CWS, findings suggest that interventions should work to improve the support a woman receives from her friends and family after losing custody to protect against increased ILDU. Providing mental health services in the wake of official custody loss may help reduce a woman's negative emotions in relation to the loss and thus protect against increased ILDU.
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WITHDRAWN

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EFFECTS OF ORAL CONTRACEPTIVE USE ON STRESS RESPONSE IN ACUTE SMOKING ABSTINENCE.

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Aims: Stress has been shown to be a predictor of smoking relapse in women. Although approximately 1 in 5 premenopausal smokers is also an oral contraceptive (OC) user, little is known about the effect of OC on stress response during smoking cessation. Therefore, we sought to compare cortisol during acute smoking abstinence in two groups – women on OC and naturally cycling women.
Methods: This is a secondary analysis from a larger controlled cross-over study including women on Tri-Sprintec (OC; n=15) and naturally cycling women (NOC; n=30). Participants quit smoking for 4 days during specific time points in their menstrual cycle: Week 1 (e.g. EE 35mg and Norgestimate0.18 mg in OC and follicular phase in NOC) and Week 3 (e.g. EE 35mg and Norgestimate0.25 mg in OC and luteal phase in NOC). Cortisol samples were collected the day before quit, quit day and on the third day of abstinence. Each day participants collected five salivary cortisol samples daily.
Results: Age was the only demographic measure significantly different between the two groups and was controlled for in the analysis (23.2 ± 6.7 vs. 29.3 ± 6.7, p=0.0027). Participants in this study smoked an average of 12.0 ± 5.5 SD cigarettes per day with an average FTND score of 3.7 ± 2.0.
The results showed that Week 1 OC users had significantly higher levels of first morning cortisol on the day before quit (28.7 ± 15.0 vs. 20.2 ± 11.4, p=0.042) whereas NOC had significantly higher levels of first morning cortisol on the third day of abstinence (18.0 ± 8.9 vs. 30.0 ± 15.3, p=0.015). During Week 3 OC had lower first morning cortisol levels on quit day compared to NOC (17.7 ± 6.8 vs. 23.5 ± 10.3, p=0.015). We also found that OC users had significantly greater change from first morning levels of cortisol to nadir (8pm) on quit day (17.4 ± 24.6 vs. 3.2 ± 14.0, p=0.037) and on the day before quit during Week 1 compared to NOC (18.4 ±15.7 vs. 10.0 ±12.8, p=0.075).
Conclusions: These finding suggest that OC use may affect cortisol levels during smoking cessation. Further studies are needed to investigate how these findings may impact smoking cessation attempts.
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HIV-1 TRANSGENIC RATS EXHIBIT ATTENUATED MOTIVATION AND ESCALATION OF COCAINE SELF-ADMINISTRATION.

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Aims: HIV-1 proteins produce neurophysiological alterations in brain regions responsible for organizing motivated behavior. The present study determined if the HIV-1 transgenic rat (Tg), a model for chronic exposure to low levels of HIV-1 proteins, exhibits altered motivation to self-administer intravenous cocaine, using both fixed-ratio (FR) and progressive ratio (PR) schedules of reinforcement.
Methods: Adult female, ovariectomized, Tg (n=14) and control (CTRL-F344; n=15;) rats were used. All rats had prior experience responding for sucrose with FR and PR schedules of reinforcement. Three self-administration phases were conducted: FR 1 schedule, 0.33 mg/kg/inj for 5 days; PR schedule, 1.0 mg/kg/inj, for 14 days; and PR schedule (0.01, 0.03, 0.1, 0.33, 1.0 mg/kg/inj), for 12 days, with FR 1 maintenance days in between each PR test. It was hypothesized that the Tg rats would be less motivated to respond for cocaine on PR schedules of reinforcement.
Results: The Tg rats self-administered fewer cocaine infusions relative to CTRLs in each phase of the experiment. Phase 1: CTRLs earned more infusions on the FR1 schedule [F(1, 19)=4.8,p<.05]. Phase 2, the CTRL rats received more cocaine infusions across all 14 days on PR [F(1, 13)=42.3,p<.001], and earned infusions increased over 14 days [F(1, 13)=5.6p<.05; cubic]. Phase 3, the PR DRC tests, animals earned more infusions as the dose increased [F(1, 13)=4.5,p=.05], and CTRL rats earned more infusions, regardless of dose, on each assessment [F(1, 13)=6.4,p<.05].
Conclusions: The present findings show that chronic exposure to HIV-related viral proteins, such as Tat and gp120, are associated with a profound motivational deficit to earn highly reinforcing stimuli such as cocaine. These findings suggest that progression through the early stage of the addiction process to cocaine will be attenuated in patients with HAND and that further studies are needed to model the late stage of the addiction process to elucidate drug abuse vulnerability associated with HAND.
Financial Support: NIH grants R01DA013137, R01HD043680, R01DA021287, T32GM081740

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POSITIVE ALLOSTERIC MODULATORS OF THE SEROTONIN 2C RECEPTOR AS NOVEL THERAPEUTICS FOR COCAINE USE DISORDER.

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Aims: The cycling course of cocaine use disorder and relapse is tied to a multitude of cognitive processes with impulsivity and cue reactivity cited as two key phenotypes that set up vulnerability to relapse even years into recovery. We reported that rats with high levels of impulsivity display low levels of 5-HT_{2C}R protein expression in the mPFC; using viral vectors to knockdown 5-HT_{2C}R expression, we confirmed that 5-HT_{2C}R loss in the mPFC leads to an increase in impulsivity and cocaine cue reactivity. These data suggest that dampened 5-HT_{2C}R signaling may play a key role in phenotypic vulnerability to relapse and that normalization of 5-HT_{2C}R function is a promising pharmacological target to promote recovery in cocaine use disorder. We synthesized new small molecules to develop 5-HT_{2C}R PAMS as a novel strategy to augment 5-HT_{2C}R signaling and suppress impulsivity and cocaine cue reactivity.
Methods: PNU-69176E was identified and found to exhibit the profile of a 5-HT_{2C}R PAM. Based on PNU-69176E, we synthesized 35 compounds and evaluated them in a Ca_i^{++} release assay and an immunoassay to detect phosphorylated $ERK_{1/2}$. Impulsivity and cocaine cue reactivity were measured using the 1-choice serial reaction time task and cocaine self-administration (0.75 mg/kg/inf, FR1-5, 14 days) and forced abstinence paradigm (1 day), respectively.
Results: CYD-1-79 potentiated 5-HT_{2C}R-induced Ca_i^{++} release and $ERK_{1/2}$ activation, with no intrinsic affinity in stably-transfected 5-HT_{2C}R-CHO cells. CYD-1-79 significantly decreased impulsive action ($p<0.05$) in the 1-CSRT task and also significantly suppressed both context-induced ($p<0.05$) and cue-reinforced ($p<0.05$) cocaine-seeking.
Conclusions: We synthesized new small molecules with the profile of 5-HT_{2C}R PAMs, one of which (CYD-1-79) suppressed both impulsive behavior and cocaine cue-reactivity. Optimization of our 5-HT_{2C}R PAMs and further evaluation of these molecules in preclinical models will allow us to develop novel pharmacotherapies for cocaine use disorder.
Financial Support: DA020087, MH093844, DA033374, DA28821, DA07287

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TRAINING IN CONTINGENCY MANAGEMENT: EFFECTS ON STAFF INTERVENTION DELIVERY SKILL, KNOWLEDGE, ADOPTION READINESS, AND ATTITUDES AFTER 90 DAYS OF IMPLEMENTATION EXPERIENCE.

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Aims: The efficacy of contingency management (CM) in addiction treatment is well-established, but less is known about impacts of training and implementation experience among community-based treatment personnel. This study reports impacts observed among an intact staff group at an opiate treatment program who underwent training followed by 90 days of trial implementation experience.
Methods: Staff (N=16) participated in a 16-hour training process, dispersed as four weekly half-day sessions at their clinic, and completed training outcome assessments one week prior and one week following training, as well as after a 90-day period of trial implementation. Assessments measured intervention delivery skill in a standardized patient scenario, conceptual knowledge, adoption readiness, and positive/negative attitudes. Repeated-measures analysis of variance (RM-ANOVA) assessed the eventual impact of training and implementation experience, with effect sizes computed and compared with those observed immediately following CM training.
Results: With exception of positive CM attitudes, RM-ANOVA revealed significant effects of training + implementation experience on each outcome. This included a robust increase in intervention delivery skill ($p<.001$, $d=2.43$), large increases in conceptual knowledge ($p<.01$, $d=.96$) and adoption readiness ($p<.01$, $d=.88$), and a similarly large decrease in negative attitudes toward CM ($p<.01$, $d=.92$). Several of these effects were of greater magnitude than those observed post-training, suggesting an additive influence of implementation experience.
Conclusions: Study findings indicate significant, durable effects of CM training—many of which were strengthened by a 90-day period of trial implementation. While replication of these findings is needed, promotional efforts for CM may be well-served by offering workshop trainings for community treatment personnel that have an applied focus and are followed by a structured period of trial implementation.
Financial Support: K23 DA025678

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PREDICTING THE EFFECTS OF D-AMPHETAMINE USING MEASURES OF SENSATION SEEKING AND IMPULSIVITY.

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Aims: This study investigated the relationship between impulsivity and sensation seeking, and the behavioral and physiological effects of d-amphetamine.
Methods: Forty young healthy adults scoring in the upper and lower median of population norms on impulsivity and sensation seeking items of the Zuckerman-Kuhlman Personality Questionnaire participated in a randomized, double-blind, placebo-controlled study designed to examine the subjective effects of oral d-amphetamine (8, 16 mg). During the first 'sample' session on each of 4 two-session blocks, subjects received 8 identical capsules all containing 0, 1 or 2 mg of d-amphetamine. During the second 'self-administration' session of each block, subjects could earn up to 8 capsules from the previously sampled d-amphetamine dose. The first capsule was earned by completing 50 responses, with the response requirement for each subsequent capsule being doubled, such that 12,750 responses were required to earn all 8 capsules.
Results: On sample sessions, sensation seeking scores were positively correlated with ratings of "good effect" ($r=.328$, $p=.039$), "high" ($r=.311$, $p=.050$), "like drug" ($r=.326$, $p=.040$) and "willing to take again" ($r=.375$, $p=.017$). Sensation seeking scores were also positively correlated with d-amphetamine capsules earned on self-administration sessions ($F1,38 = 5.387$, $p=.026$, $r2=.124$). Impulsivity was not significantly correlated with any of the behavioral or physiological effects of d-amphetamine.
Conclusions: Individuals with higher sensation seeking scores are more likely to experience d-amphetamine effects favorably and work harder to obtain d-amphetamine. Sensation seeking, but not impulsivity, predicted initial amphetamine use.
Financial Support: Supported by DA-05312

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AGREEMENT BETWEEN TIMELINE FOLLOW-BACK (TLFB) AND AUDIO COMPUTER-ASSISTED SELF INTERVIEW (A-CASI) IN HIV PRIMARY CARE PATIENTS: ASSESSMENT OF DAYS USED PRIMARY DRUG.

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Aims: The interviewer-administered Timeline Follow-Back (TLFB) and the Audio Computer-Assisted Self Interview (A-CASI) are two of the most widely used patient reporting methods to measure outcome data in clinical studies. TLFB uses a calendar and other reminder techniques; A-CASI provides greater privacy in the reporting situation. Each technique is assumed to improve reporting, but little is known about the agreement of these two different methods of reporting.
Methods: Prior to randomization into an on-going clinical trial of brief interventions to reduce non-injection drug abuse in HIV primary care patients, baseline assessments using both of these methods were conducted in 200 patients (largely African-American or Hispanic) in urban HIV primary care. TLFBs on primary abused substance were administered by trained study counselors (experienced HIV health educators), yielding days used in the prior 30 days. A-CASI questions simply asked patients how many days they used the drug in the prior 30 days. Intraclass correlation coefficients (ICC) indicated level of chance-corrected agreement (ICC ≥.75 indicates excellent agreement).
Results: Overall agreement between the two methods was excellent (ICC=.81), with little variation by primary drug (cocaine, methamphetamine, or heroin, ICC=.80; .79; .89), by gender (male, female=.80; .82), or ethnicity (Hispanic vs. other, ICC=.88; .78). However, agreement was only fair (ICC=.62) among binge drinkers (~28% of the sample), compared to excellent agreement (ICC=.85) among the others.
Conclusions: TLFB and A-CASI assessments showed high agreement in a baseline assessment of days used primary drug in the prior 30 days, suggesting that different aspects of the procedures did not greatly add to or detract from patient reports. However, the lower agreement of measures among drug user/binge drinkers suggests the need for additional attention to measurement, and perhaps intervention methods in this group.
Financial Support: Grants R01DA024606, R01AA014323, K05AA014223, and NYSPI

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ROUTES OF ADMINISTRATION AND FREQUENCY OF ABUSE OF OXYCONTIN® AND IMMEDIATE-RELEASE OXYCODONE IN A RURAL KENTUCKY COUNTY FOLLOWING INTRODUCTION OF REFORMULATED OXYCONTIN: RESULTS FROM THE FIRST 71 FOLLOW-UP INTERVIEWS.

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Aims: In August 2010, Purdue Pharma introduced reformulated OxyContin (ORF) intended to deter abuse particularly through routes that require tampering, including snorting or injecting. This study describes changes in abuse approximately 2-2.5 years following the introduction of ORF in a sample of OxyContin abusers originally identified in 2010-2011.
Methods: Structured follow-up interviews conducted August 2013-October 2013, assessing opioid abuse, including past 30-day routes of administration (ROA) and frequency, were conducted in individuals who abused original OxyContin (OC) prior to August 2010 in rural Kentucky. The first 71 re-interviews of the original study population (n=189) are completed; additional re-interviews are ongoing.
Results: Although 77% (n=55) of re-interviewees retrospectively reported that OC had been their preferred drug prior to the reformulation, among the 71 follow-up interviews, only 1 individual (1.4%) reported oral abuse of ORF in the past 30-days and no abuse via non-oral ROA was reported. In contrast, 53.5% reported past 30-day abuse of immediate-release (IR) oxycodone (12.5 days/month), mainly via snorting and injecting ROA. When asked about their preferred drug now that OC was not on the market, 0% selected ORF as their current preferred drug, compared to 45% who selected single-entity IR oxycodone, 29% who selected Suboxone®/Subutex®, and 11% who selected methadone as preferred drugs. Only one individual (1.4%) reported attempting to manipulate ORF for non-oral abuse.
Conclusions: While OC was retrospectively reported to be the preferred drug for the majority of individuals before ORF introduction, none reported preferring ORF at the follow-up interviews, and only 1 individual reported abuse of ORF in the past 30-days. These results indicate that reformulated OxyContin has deterred abuse in this community in the 2 years after its introduction.
Financial Support: Purdue Pharma

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FAMILY/SOCIAL PROBLEMS AS A GREATER BARRIER TO TREATMENT ENTRY FOR WOMEN THAN MEN.

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Aims: There is a well-established gender disparity in substance use treatment with women less likely to enter and stay in treatment. Despite previous research investigating this disparity, gender specific models predicting treatment initiation have not been reliably established. This study examines impulsivity, depression, family/social problems, and drug severity as predictors of treatment entry in cocaine dependent adults presenting to an addictions treatment research clinic in Houston TX. It was hypothesized that these factors would negatively predict treatment entry, but that the association would be greater for women than for men.
Methods: Participants completed the Addiction Severity Index (ASI), Barratt Impulsivity Scale (BIS-11) and Beck Depression Inventory (BDI-II) as part of the intake process. Analyses included only observations with complete data on all measures (n= 416; n = 94 females, n = 322 males).
Results: Bayesian logistic regression was utilized to evaluate whether gender, impulsivity, family/ social problems, drug severity and depression predicted attendance at the first treatment visit. Results indicated that there was a 98.2% chance that an interaction between gender and family/social problems existed. Among men, family/social problems increased the odds of failing to attend the first treatment visit (O.R. = 2.63, 95% CI = 13.91- 11.86); whereas among women, family/social problems had a stronger predictive value (O.R. = 86.30, 95% CI = 4.97-2267.20). Although the wide credible interval for women means that the estimation of the odds ratio may lack precision, inspection of the Bayesian posterior distribution analysis indicates that there is a 76.66% chance that the effect for women exceeds an O.R. = 2.
Conclusions: Family/social problems negatively predict initial treatment attendance. While this effect was significant for both males and females, odds ratios were substantially greater among females. The results provide initial estimates of gender and familial health-care disparities that may be important factors to consider in the design of clinical trials and treatment platforms.
Financial Support: None

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RELIABILITY OF PUPIL DIAMETER MEASUREMENTS IN NEONATES.

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Aims: Pupil diameter is a sensitive, objective index of opioid effects in adult humans, but to our knowledge, has not been examined in neonates, despite the potential for this information to improve the assessment and treatment of neonatal abstinence syndrome (NAS) in neonates exposed to opioids in utero. To begin to test this idea, a prior study of ours examined infant pupillary response to methadone administration during treatment for NAS in 10 neonates (Heil et al., 2012). A picture of one of each infant's eyes was taken under controlled illumination conditions with a standard digital camera just prior to dosing and approximately 0.5, 3, 6, and 9 hours after dosing. ImageJ software was used to measure the diameter of the pupil and iris in the digital picture files. Relative pupil diameter (pupil diameter ÷ iris diameter) was calculated and analyzed. Like adult pupils, neonatal pupils constricted rapidly after dosing, then gradually dilated over the rest of the observation period. These data demonstrated the feasibility of measuring pupil diameter in neonates and provided some initial validity data. Before conducting further validity studies, the present study set out to formally test the reliability of our neonatal pupil photography protocol.
Methods: For inclusion in this ongoing study, neonates must be full term and have no obvious ocular problems or any other conditions that would obviate pupil measurements. Three photographers photograph the same eye of each neonate during one session in the first 48 hours after delivery using the same procedures as in our earlier study. Reliability is computed based on intraclass correlation coefficients computed from the derived variance components.
Results: Data have been collected from 33 infants to date, 24 opioid-exposed and 9 non-exposed. Preliminary analyses indicate that the intraclass correlation coefficients average 0.76, suggesting that this protocol has adequate reliability.
Conclusions: Further studies of the validity of pupil diameter as a measure of NAS using this procedure are warranted.
Financial Support: Supported by R01 DA031928 and T32 DA07242 from the National Institute on Drug Abuse.

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PRELIMINARY RESULTS FROM A STUDY EVALUATING CREATINE AS A TREATMENT OPTION FOR DEPRESSION IN FEMALE METHAMPHETAMINE USERS.

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Aims: The aim of this pilot study is to evaluate changes in Hamilton Depression Rating Scale (HAMD) & Beck Anxiety Inventory (BAI) scores over the course of 8 weeks of creatine treatment in a sample of depressed female methamphetamine (MA) users. Research has identified several sex-based differences in MA use disorders. Notably, female MA users report higher levels of depressive & anxiety symptoms than males, & this comorbidity confounds treatment outcomes. Despite considerable support for the importance of both depression & anxiety in the context of MA use disorders, the evidence suggests that antidepressants prescribed to patients with MA dependence are either ineffective or have unacceptable side-effect profiles. The literature suggests that creatine is a safe hypothesis-driven strategy for reducing both depression & anxiety. Therefore, we hypothesize that there will be a decrease in HAMD & BAI scores with creatine treatment.
Methods: Eligibility criteria include current major depressive disorder, MA dependence, & HAMD > 15. To date, 10 subjects have been enrolled and treated with 8 weeks of open-label creatine. Six have completed, 3 are in progress, & 1 dropped-out. Recruitment is ongoing. Treatment response is measured with the HAMD & BAI.
Results: Preliminary findings indicate that the mean (±sd) HAMD & BAI scores for those who completed the 8 week intervention (n=6) were reduced from 17.7 (±1.6) & 22.8 (±8.8) to 5.7 (±4.1) & 4.2 (±3.6), respectively. Analyses reveal that HAMD and BAI scores significantly decreased starting after 2 weeks (p=0.025) & 1 week (p=0.023), respectively. There have been few side effects reported, & none are thought to be related to study participation. Three of the completed women requested to continue creatine upon study completion.
Conclusions: Preliminary evidence from this longitudinal, intervention study of a single cohort of MA dependent females suggests that oral creatine may result in reduced depression & anxiety symptoms. Based on these preliminary results, a larger scale trial is warranted.
Financial Support: Support provided by 5R01DA027135 & K05DA031247.

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LOCUS-SPECIFIC EPIGENETIC REPROGRAMMING FOR THE STUDY OF REWARD PATHOLOGY.

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Aims: Genome-wide assessments of histone posttranslational modifications (HPTMs) have identified drug regulation at numerous target genes implicated in the associated behavioral abnormalities. However, it has not previously been possible to manipulate the epigenome in order to causally link the chromatin state of a single locus with behavioral and molecular responses to psychostimulant exposure. Engineered transcription factors can direct enzymatic moieties to specific genomic loci. We are interested in epigenetic regulation of the immediate early gene, FosB, which is both necessary and sufficient for many of the downstream molecular changes mediating drug response.
Methods: Zinc finger proteins (ZFPs) were designed to recognize the FosB promoter and tethered to the catalytic domains p65 or G9a. For in vivo analysis, mouse NAc neurons were infected with herpes simplex virus (HSV) expressing each of the constructs, and qRT-PCR and immunohistochemistry was used to determine activation or repression of FosB expression. We relied on qChIP using a variety of anti-HPTM antibodies to analyze the chromatin modifications induced by the ZFP-G9a and ZFP-p65 constructs. To determine the role of epigenetic remodeling on behavioral responses to psychostimulant exposure, mice were subject to cocaine locomotor sensitization.
Results: We have found that HSV-FosB-ZFP-p65 and -G9a regulate FosB/ΔFosB expression in NAc neurons. HSV-FosB-ZFP-G9a methylates histones specifically at the FosB gene in vivo, while FosB-ZFP-p65 acetylates these histones. Engineered transcription factors are also able to modulate behavior, as FosB-ZFP-p65 expression in the NAc enhances cocaine locomotor sensitization, while FosB-ZFP-G9a expression blocks the cocaine effect on locomotor as well as sensitizes animals to stress.
Conclusions: Engineered transcription factors are effective tools to probe the behavioral and molecular consequences of chromatin remodeling at a single locus in vivo.
Financial Support: Supported by NIDA (1F32DA035518-01) and NIMH.

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NEUROBIOLOGICAL AND SUBJECTIVE STRESS REACTIVITY AMONG INDIVIDUALS WITH PRESCRIPTION OPIOID DEPENDENCE: WHAT IS THE ROLE OF INTERPERSONAL TRAUMA EXPOSURE?

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Aims: Research examining stress reactivity among prescription opioid (PO) dependent individuals is scant. Both addiction and trauma are known to influence HPA axis functioning, but their combined effects are rarely explored. We examined within and between group differences in response to the Trier Social Stress Task (TSST) among PO individuals (n=19) and healthy controls (n=19). We hypothesized that 1) the PO and control group would demonstrate increases in stress reactivity in response to the TSST and 2) the PO group would demonstrate greater stress reactivity compared to controls. We also examined whether interpersonal trauma history moderated between-group differences.
Methods: Heart rate, galvanic skin response (GSR), salivary cortisol, dehydroepiandrosterone (DHEA), and subjective ratings of craving, stress, anger, sadness, happiness and anxiety were measured before and immediately after the TSST.
Results: Controls demonstrated increased GSR, stress, anger, and anxiety in response to the TSSR. PO individuals demonstrated increased cortisol, DHEA, craving, stress, and anger and decreased happiness. In comparison to controls, the PO group demonstrated greater GSR and DHEA, craving, stress, anger, sadness, and anxiety and less happiness in response to the TSSR. No significant moderations emerged. Post-hoc analyses among the PO group indicated that emotional abuse was negatively correlated with cortisol and DHEA reactivity; witnessing family violence was positively correlated with anger reactivity; and lifetime physical abuse was positively correlated with sadness reactivity.
Conclusions: Stress reactivity was amplified among the PO group in this sample. Interpersonal trauma and PO dependence may have differential effects on stress reactivity. The combined influence of addiction and interpersonal trauma on stress reactivity remains an important area for future study.
Financial Support: K23 DA021228 (SEB) and K12 HD055885 (KTB).

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ANALYZING DISPARITIES ON TOBACCO USE THROUGH CBPR.

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Aims: This study adds to the chain of epidemiologic evidence that describes how tobacco use disproportionally affects underserved populations. However, many of these populations are under-represented in research due to mistrust and disenfranchisement. We used a Community-Based Participatory Research approach to develop survey methods, instruments and analyses that address this lack of representation.
Methods: A total of 3,901 people were surveyed in different locations of an urban community of the Mid-Atlantic region with a relatively heterogeneous population (corresponding to 2,554 residents and 1,377 community visitors). Of note is that a third of the white (W) and African American (AA) population has an annual income below the federal poverty level. Survey sites were selected to reflect this heterogeneity by community members organized in a taskforce.
Results: Smoking among residents was twice as high compared to visitors (56% vs. 27%, p <0.001). Important differences were also observed by gender (66% of men residents and 45% female residents smoke, vs. 39% and 19%, respectively, among visitors), and race (61% among AA residents and 35% among AA visitors were current smokers, vs. 45% among W in residents and 17% among W visitors). Multivariate analysis confirmed these differences are independent of education attainment, age, and occupation status. A third of all currently smoking participants wanted to quit smoking immediately (36%), and a quarter in the next 6 months (24%).
Conclusions: The data shows that important disparities still exist regarding tobacco use by race, gender, and socio-economic status. Better than half of people who smoke are looking forward to quitting smoking, even among underserved communities. CBPR may be needed to help develop knowledge and interventions to address these disparities.
Financial Support: Supported by grant R24 MD002803 from the National Institute of Minority Health and Health Disparities.

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PRENATAL STIMULANT EXPOSURE ALTERS INFANT GROWTH IN-TERM BORN INFANTS.

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Aims: Prenatal exposure to stimulants (PSE), including prenatal methamphetamine (MA) and/or tobacco (TOB), is associated with fetal growth restriction. However, less is known regarding the growth of infants with PSE during the early postnatal period. The aim is to investigate the effects of PSE and sex on growth trajectories of infants over the first 3 months of age.
Methods: 169 infant-mother pairs were investigated for birth measurements and growth parameters. 85 PSE infants (born 38.9±0.2 weeks gestation, 48 boys, 39 MA+TOB, 37 TOB only, 2 MA only, and 7 MA+alcohol) and 84 control infants without drug exposure (CON) (39.1±0.16 weeks gestation, 36 boys). Length, weight, head circumference, and BMI were collected at birth, 1 week, 1 month, and 2-3 months old. Exposure status was determined by maternal self-report and birth records.
Results: At birth, PSE infants were shorter (p=0.05), weighed slightly less (p=0.07), had lower BMI (p=0.01) and slightly smaller head circumference (p=0.11) than CON infants. During the 3-months, PSE infants also gained less weight than CON (p=0.008). Other growth parameters were not different. PSE girls gained weight less quickly than CON girls (p=0.003), but this was not seen among the boys (3-way interaction-p<0.06). PSE girls also tended to grow in length slower than CON girls (p=0.2).
Conclusions: Although these infants were all term-born, those with PSE were smaller at birth and had a slower growth rate during the early postnatal period. Animal studies on PSE showed that both male and female rat pups gained less weight than their exposed counterparts. PSE children also were shorter than unexposed children, but findings on sex-specific drug effects are sparse. During early infancy, only PSE girls gained less weight, suggesting that girls are more vulnerable to the effects of stimulant exposure than boys. Follow-up studies are in progress to evaluate possible epigenetic effects or other co-morbid factors to PSE and their associations with infant growth.
Financial Support: NIH (2K24-DA16170, U54-NS56883, G12-MD007601)

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UNDERSTANDING DRUG USE AND THE HIV CASCADE OF CARE IN SAN JUAN, PUERTO RICO.

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Aims: This presentation will highlight barriers to linkage to HIV care among IDUs based on pre-implementation results of Proyecto PACTo (PPo), a clinical trial that aims to implement and evaluate in a community-level, structured approach to enhance HIV care access and retention for substance users in San Juan, Puerto Rico.
Methods: A rapid ethnographic approach was used to inform the recruitment of HIV-infected drug users into PPo and to describe the HIV cascade of care in a culturally and contextually situated manner. The fieldwork entailed participant observations of syringe exchange outreach to shooting galleries and other venues, over 35 informal conversations and 150+ encounters with members of the target population that were captured in detailed field notes and photographs and later analyzed for recurrent themes.
Results: Many of the HIV-positive IDUs reported not receiving regular medical attention or adhering to an HIV treatment regimen because they felt "discriminated against" and "marginalized" in clinic and hospital settings. They also face a myriad of challenges that hinder retention in HIV care including co-morbid conditions of substance use and mental health disorders, lack of social support, stigma and discrimination, and poverty-related issues such as unstable housing and food insecurity. Detoxification narratives were quite prominent with many of the street-based drug users commonly describing previous unsuccessful attempts and present desires to enroll in drug treatment programs but cited limited options and costs as key impediments.
Conclusions: Efforts to address the HIV cascade of care in this population must also address social and structural forces that act as barriers to HIV prevention, care and treatment.
Financial Support: NIDA R01-DA035280

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MATERNAL IMPULSIVITY AS A PREDICTOR OF ADOLESCENT SMOKING STATUS.

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Aims: Previous research has confirmed that adolescent smoking behaviors are impacted by a number of parenting variables, including parental smoking status. Further, smoking behaviors have consistently been linked to behavioral measures of impulsivity in both adolescents and adults. To date, there are no studies that indicate whether parental measures of behavioral impulsivity can directly predict adolescent smoking status.
Methods: The current work represents sub-analyses of a larger investigation at Nationwide Children's Hospital that required 56 mother and adolescent (41% male; Mage=14.29) dyads to complete a number of behavioral tasks and self-report measures. To investigate the relationship between maternal impulsivity and adolescent smoking status, data from the Delay Discounting Questionnaire (DDQ), Conners' Continuous Performance Test (CPT), and the Go-Stop Task were used to predict child smoking status classification, (1)never smoked, (2) tried smoking in the past and, (3) current smoker.
Results: Results from a one-way ANOVA indicate that the Go-Stop Task ($F(2, 52)=.709$, $p=0.497$) and CPT Ommissions ($F(2, 42)=1.426$, $p=0.250$) were not significantly related to adolescent smoking status. Performance on the DDQ ($F(2,53)=3.437$, $p=0.039$) and CPT Omissions ($F(2,52)= 6.032$, $p=.004$) were significantly related to child smoking status, such that parents whose performance indicated low levels of impulsivity had adolescents who were non-smokers and those with high impulsivity had adolescents who were current smokers.
Conclusions: Findings suggest that maternal impulsivity may be a risk factor for adolescent smoking status. Further, it is hypothesized that maternal impulsivity may impact parenting behaviors which highly correlate to adolescent smoking status. Future research should investigate parental monitoring and family functioning as potential mediators of this relationship.
Financial Support: None

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ENHANCING THE EFFECTS OF COGNITIVE BEHAVIORAL THERAPY FOR PTSD AND ALCOHOL USE DISORDERS WITH ANTIDEPRESSANT MEDICATION: A RANDOMIZED CLINICAL TRIAL.

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Aims: This study compared the efficacy of trauma focused therapy, Seeking Safety (SS) and its combination with antidepressant medication (sertraline) on the treatment of co-occurring posttraumatic stress disorder (PTSD) and alcohol use disorders (AUD).
Methods: Study was a double-blind, randomized clinical trial of 69 participants who met DSM-IV TR criteria for PTSD and AUD. The inner-city sample was notable for the chronicity of traumatic stress exposure and prevalence of comorbid substance use disorders. Participants were randomly assigned to SS plus sertraline (n=32) or SS plus pill placebo (n=37). This version of SS consisted of 12 weekly individual sessions of 60-minute duration. Clinician Administered PTSD Scale (CAPS) and the Modified PTSD Symptom Scale-Self Report (MPSSR) were used to assess PTSD diagnosis and severity. Drinking patterns and rates were assessed with Time Line Follow-Back Interview. Evaluations blind to treatment assignment were conducted prior to treatment and at 1-week and 6-months posttreatment.
Results: Model analyses demonstrated that participants treated with combination SS and sertraline experienced significantly greater improvement in PTSD symptoms than those treated with SS and pill placebo at posttreatment as measured by CAPS ($\chi2(1) = 4.08$, $p < 0.05$). Significant difference in PTSD improvement continued at 6-month follow-up. Participants in both treatment groups improved significantly on AUD severity outcomes with no difference between SS and sertraline and SS and placebo treatment.
Conclusions: Combined Seeking Safety and sertraline treatment was more effective for PTSD than Seeking Safety with placebo in an urban sample of co-occurring PTSD and AUD. This is the first controlled trial to follow and demonstrate differential benefits in PTSD improvement at 6-months posttreatment for combined treatment medication and Seeking Safety. Both groups experienced significant reductions in AUD severity sustained at 6-month follow-up.
Financial Support: Study supported by R01AA014341 from the NIAAA (PI: Denise A. Hien, PhD).

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"I TAKE MY REFUGE IN TIK": UNDERSTANDING GENDER DIFFERENCES IN THE INITIATION OF METHAMPHETAMINE USE IN SOUTH AFRICA.

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Aims: South Africa has a growing epidemic of methamphetamine use (commonly referred to as tik in South Africa). Tik impacts nearly every area of a users' life, deteriorating both personal and social functioning. The aim of the current study was to better understand gender differences in initiating tik use in Cape Town, South African.
Methods: As part of a larger study examining tik use and HIV risk, 15 female and 15 male tik users from Cape Town, South Africa were recruited for in-depth qualitative interviews. Analytic memos were written for each transcript in order to summarize emerging themes and identify in vivo codes, terms, and interpretations in participants' own words.
Results: A distinct pattern emerged between men and women's responses, particularly among the Coloured participants. Women were more likely to report that their tik use originated as a coping strategy to manage negative emotions after a traumatic experience. Traumatic experiences included an unwanted abortion, being left by her husband, sexual abuse by a neighbor, and her father burning her house down, among others. One woman explained, "Anytime I have painful memories, I take my refuge in tik." In contrast, the men, and surprisingly the Black women, consistently identified friends as the reason for using tik, with the underlying goal of trying to fit in. One man referred to the social pressure he felt to begin using tik, "All my friends started using tik. I was the only one who was not smoking…".
Conclusions: The accounts of these individuals have implications for the development of interventions aimed at preventing the initiation of tik use in South Africa. Specifically, Coloured women may benefit from learning skills to manage negative affective states after traumatic experiences, while men and Black women may benefit from learning skills to overcome social pressure to use tik.
Financial Support: This study was supported by grants from National Institutes on Drug Abuse (K23 DA028660, R03 DA033828).

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ASSOCIATIONS OF SMOKING HISTORY WITH CIGARETTE SMOKING EXPECTANCIES AMONG ADULTS IN RESIDENTIAL SUBSTANCE USE TREATMENT.

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Aims: Cigarette smoking is problematic among adults in residential substance use treatment, with prevalence ranging from 70-90%. Social learning theory suggests that individuals smoke cigarettes in part due to expectations for positive or negative reinforcement. Smoking expectancies have been examined in several populations of smokers including adolescent and adult substance users. The current study aims to extend previous work and to examine the relationship between smoking history and smoking expectancies in a population of adults in residential treatment for substance use.
Methods: We administered the Short-Smoking Consequences Questionnaire to, and collected several smoking history variables from participants (n=40).
Results: At a univariate level, positive smoking expectancies (positive and negative reinforcement) were significantly related to years of regular smoking ($r=.41$, $p=.01$), time to first cigarette in the morning ($r=.47$, $p=.001$), smoking in the past 30 days ($r=.37$, $p=.03$), and cigarettes per day before entering a restricted environment ($r=.73$, $p=.01$). Expectancies were also associated with Cannabis Dependence ($r=.39$, $p=.01$), and Cocaine Dependence ($r=.36$, $p=.02$). Results of a multiple linear regression analysis indicated positive expectancies were significantly related to longer-term smoking characteristics, years of regular smoking ($F(1,34)=4.62$, $p=.03$, $R=.12$) and time to first cigarette in the morning ($F(1,32)=5.09$, $p=.03$, $R=.28$), but not to current smoking behavior. Cannabis and Cocaine Dependence did not account for additional variance in the multivariate model.
Conclusions: Results are consistent with previous work in substance using adolescents and adult smokers that suggest positive expectancies are significantly related to stable smoking behavior variables and indices of nicotine dependence. Results support the utility of examining smoking outcome expectancies in adult inpatient substance users and the need to incorporate this construct into larger integrated models of smoking outcomes in this population.
Financial Support: No direct financial support for this research.

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REARING ENVIRONMENT MODULATES THE EFFECT OF A GLUCOCORTICOID RECEPTOR ANTAGONIST ON COCAINE SELF-ADMINISTRATION IN RATS.

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Aims: Isolation rearing is often used as a model of early life stress in rodents. Consistent with other chronic stressors applied early after weaning, isolation rearing increases stimulant self-administration. Studies suggest that the stress hormone corticosterone and its receptor, the glucocorticoid receptor (GR), modulate self-administration. The present studies tested the hypothesis that rats raised in isolation (IC) would demonstrate a diminished response to a GR antagonist and would express decreased GR in the stress-relevant prefrontal cortex compared to rats raised in an enriched environment (EC).
Methods: For experiment 1, male Sprague-Dawley rats were placed in IC (n=7) and EC (n=7) conditions immediately following weaning. Rats were then trained to self-administer cocaine (0.03, 0.1, or 0.3 mg/kg) on a FR1 schedule. Once stability was reached, rats were pretreated with the GR antagonist, RU486 (20 mg/kg, s.c.) or vehicle. Responding after RU486 administration was analyzed using a 2 x 3 mixed ANOVA. For experiment 2, a separate group of rats were placed in IC (n=10) and EC (n=10) conditions as before. Rats were then killed and medial prefrontal cortex, orbitofrontal cortex, and amygdala were removed. Western blot analysis was used to semi-quantify levels of GR expression. Data were analyzed using separate t-tests for each brain region.
Results: A significant interaction was found in experiment 1. At 0.03 mg/kg cocaine, EC rats demonstrated a significantly greater decrease in cocaine self-administration after RU486 than IC rats; however, at 0.1 mg/kg cocaine, IC rats showed a greater decrease. No significant differences in GR expression were found in any brain area examined.
Conclusions: In general, blocking the stress axis with RU486 decreased self-administration of cocaine; however, this effect was cocaine dose- and environment-dependent. The subsensitivity to RU486 observed in IC rats at a low unit dose of cocaine may reflect GR overactivity by corticosterone rather than a specific alteration in GR protein expression.
Financial Support: Supported by: DA012964 and DA016176

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EMPLOYMENT-BASED REINFORCEMENT OF OPIATE AND COCAINE ABSTINENCE IN OUT-OF-TREATMENT INJECTION DRUG USERS.

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Aims: A recent clinical trial examined whether employment-based reinforcement could promote enrollment in methadone treatment and drug abstinence in out-of-treatment injection drug users. The intent-to-treat analysis showed that the abstinence reinforcement contingencies had only modest effects on drug abstinence. This appeared to result from the fact that not all participants were exposed to the abstinence contingencies. The present study provides a more focused assessment by restricting the analysis to participants who were actually exposed to the abstinence contingencies.
Methods: Out-of-treatment injection drug users were invited to work in the Therapeutic Workplace, a model employment-based program for drug addiction. Participants (n=33) could work for 4 hr every weekday for 30 weeks and earn about $10 per hr. During a 4-week induction, participants could work and earn maximum pay independent of their treatment status and drug use. After induction, access to the workplace was contingent on enrollment in methadone treatment. After participants met the methadone enrollment contingency for three weeks, participants had to provide opiate-negative urine samples to maintain maximum pay. After participants met those contingencies for three weeks, participants had to provide opiate- and cocaine-negative urine samples.
Results: The percentage of thrice-weekly urine samples that were negative for opiates and cocaine remained stable until the abstinence reinforcement contingency for each drug was applied. The percentage of opiate- and cocaine-negative urine samples increased abruptly and significantly after the opiate and cocaine abstinence contingencies, respectively, were applied.
Conclusions: Employment-based abstinence reinforcement can increase opiate and cocaine abstinence among out-of-treatment injection drug users.
Financial Support: R01DA023864, K24DA023186, & T32DA07209

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MANAGING AND IMPROVING BEHAVIORAL HEALTH CARE QUALITY IN PRIVATE HEALTH PLANS.

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Aims: Health plans play a key role in promoting behavioral health care quality. The study aim was to determine national estimates of private health plans' activities related to behavioral health care quality, including incentives and recognition programs.
Methods: Data are from the 2010 Brandeis Health Plan Survey on Alcohol, Drug and Mental Health Services, a nationally representative survey of private health plans regarding behavioral health care. We sampled private health plans in 60 market areas to obtain data on each market-specific plan's top 3 commercial products, reporting here on 385 plans (88% response) completing the quality improvement module. We conducted product-level univariate and bivariate analyses (n=925 products) with weighted data.
Results: Over 96% of health plan products conducted patient surveys regarding behavioral health services. Most reported aggregated results to providers and purchasers. Tracking the National Committee on Quality Assurance's HEDIS behavioral health measures was also nearly universal (97%), with results commonly reported to providers, purchasers and enrollees. About one-third had provider incentives or recognition programs tied to performance measures. About one-third of products required providers to use standardized instruments to assess clinical outcomes for behavioral health patients with 72% of those reporting results to individual providers and 65% reporting aggregated results to both enrollees and purchasers.
Conclusions: Results provide an important picture of private health plans' activities regarding behavioral health care quality. Many plans have begun using incentives and recognition programs in keeping with general medical care trends, but there is room to grow in use of these approaches.
Financial Support: National Institute on Drug Abuse R01 DA029316, National Institute on Alcohol Abuse and Alcoholism R01 AA010869.

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DIFFERENTIAL INFLUENCE OF PRENATAL MATERNAL AGGRESSION ON CHILDHOOD EXTERNALIZING SYMPTOMS AND ADOLESCENT SUBSTANCE USE BY GENDER.

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Aims: Girls with externalizing symptoms have a higher risk of developing substance use problems than boys with externalizing symptoms, but the etiology is unclear. We hypothesized that mother's aggressive reactivity during pregnancy (known to elevate HPA axis activity and increase risk for offspring ADHD) predicts offspring externalizing disorder in childhood, which in turn predicts substance use in adolescence; also, females would be more affected due to known differential exposure to maternal cortisol for females in utero.
Methods: 413 pregnant teenager and offspring dyads recruited from an urban clinic were assessed during early pregnancy and at 6- and 16-year follow-ups. Offspring externalizing symptoms and drug use were assessed at 6- and 16-years, respectively. A multi-group SEM was performed on the model for each gender using mean and variance adjusted weighted least squares estimation method, with covariates ethnicity, mother's age and prenatal alcohol use.
Results: There was good model-data fit for females, 2(3, N=180)=1.22, p=.750, CFI= 1.00, RMSEA=.00, and males 2(3 N=191)=50,p=919,CFI=1.00, RMSEA=.00. For females, maternal aggression during pregnancy predicted maternal aggression and offspring externalizing symptoms at offspring age 6. Female offspring were more likely to use substances (marijuana 30%, alcohol 24%, cigarette 35%) at age 16 for one SD increase in age 6 externalizing symptoms. For males, maternal aggression during pregnancy predicted maternal aggression 6-years later but not offspring externalizing age 6. Males were 27% more likely to use cigarettes at age 16 for one SD increase in age 6 externalizing, but there was no relation to marijuana or alcohol use.
Conclusions: Results demonstrate a potential differential relation between prenatal maternal aggressive reactivity and longer term offspring outcomes of externalizing symptoms and substance use by offspring gender. Additional studies are warranted to determine the mechanisms driving these relationships.
Financial Support: DA000357 (PI:Horner); AA08284, DA009275, AA022473 (PI:Cornelius); DA005605 (PI:Tarter)

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UNDERSTANDING THE PREDICTIVE VALUE OF ABUSE POTENTIAL ASSESSMENTS.

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Aims: With the dramatic rise in prescription drug abuse, regulatory focus has increased on understanding the abuse potential of novel drugs. Abuse potential assessment is comprised of multiple models ranging from in vitro experiments through clinical studies and epidemiological data. Previous work from our group utilized a translational pharmacology approach to understand the predictive value of these models in their ability to predict scheduling status and outcomes of human subjective effect studies. The current work extends upon these findings by assessing the predictive value of these models following stratification by drug class or scheduling status.
Methods: The analysis included literature findings and in-house data from 100 drugs in which scheduling decisions have been rendered, stratified by pharmacological mechanism or scheduling status. For statistical analysis, we utilized binary classifications to classify all drugs comparing the results of specific models (in vitro binding activity, functional activity, rodent locomotor activity, rodent drug discrimination, rodent self-administration fixed ratio and progressive ratio, and human subjective effects studies) to scheduling status and the outcome of human subjective effect studies. From this data, statistical endpoints such as concordance, sensitivity, specificity, and positive/negative predictive value were calculated to make objective comparisons on the diagnostic value of these models.
Conclusions: Initial findings revealed that the preclinical drug discrimination and self-administration assays as well as the clinical subjective effect study provided the most predictive value of all of the models considered. Further analysis of these models with respect to drug class and scheduling status provides greater resolution as to whether certain abuse potential models are more or less predictive depending on the pharmacological mechanism or scheduling status of the compound. These data provide insight into opportunities to focus future efforts to improve our capability to predict abuse potential in an experimental setting.
Financial Support: This work was funded by Pfizer, Inc.

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MOBILE INTERVENTIONS BASED ON ECOLOGICAL MOMENTARY ASSESSMENT: PERSPECTIVES OF PATIENTS AND PROVIDERS IN CHINA, TAIWAN, AND THE UNITED STATES.

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Aims: Aim: The tracking of mood and behavior via smartphones provides EMA or real-time assessments which can be used to develop individualized interventions delivered timely to assist those in need. This study investigates perspectives of patients and providers in China, Taiwan, and USA regarding smartphone applications for substance abuse.
Methods: Methods: Focus groups were conducted with patients (N=71) and providers (N=22) in methadone maintenance treatment (MMT) in China, Taiwan, and the United States. All focus groups were audio taped and transcribed. Atlas.ti7 was used to analyze data.
Results: Results: Most participants were open to answering daily surveys and having a tool within their phone; US participants seemed to think having a live person they could text or talk to would be best. When experiencing a "trigger" situation and are tempted to use, some participants expressed unwillingness to answer survey questions in the moment but suggested willingness after some time when the craving has passed. All participants expressed an interest in progress charts showing their use/non-use over time. Some participants wanted to see health tips/alternatives for those trying to wean off of MMT; foods that may affect the liver or kidney; health tips for those with HCV, cigarette smokers, and those with chronic pain. Relatively speaking, more patients in China and Taiwan had reservation on the intervention but felt that inclusion of family support be helpful, while most US patients were involved in self-help groups and emphasized the need for assistance with locating meetings, connecting with sponsors, or AA/NA directory.
Conclusions: Conclusions: Smartphone applications can timely deliver individualized interventions when and where the user needs it most, but local cultural variations need to be taken into consideration to optimize the impact and effectiveness.
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WITHDRAWN

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ASSOCIATIONS BETWEEN BLOOD LEAD LEVEL AND SUBSTANCE USE AMONG ADULTS IN THE UNITED STATES.

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Aims: The adverse effects of lead exposure on cognitive function and impulse control are well established. However, the relationship between lead exposure and risk-taking behavior such as use of alcohol and drugs - behaviors directly influenced by deficits in cognitive function and impulse control - has received little attention. The aim of this study is to measure the association between lead exposure and substance use in United States.
Methods: We used the National Health and Nutrition Examination Survey (NHANES) to examine the associations between blood lead and binge drinking (1999-2010, N=26,938) and drug use (2005-2010, N=9,304) including use of marijuana, cocaine, heroin, methamphetamine, and injection drugs among adults aged 20-59 years old.
Results: After adjusting for gender, age, race/ethnicity, education, poverty, and smoking, adults with blood lead levels in the highest quintile had elevated odds of lifetime binge drinking [odds ratio (OR): 1.61, 95% CI: 1.33-1.95] and report of any binge drinking (OR: 1.91, 95% CI: 1.64-2.22) and frequent binge drinking (OR: 2.00, 95% CI: 1.67-2.38) in the past 12 months. Significant associations were also observed between blood lead and any previous drug use (OR for highest quartile: 1.47, 95% CI: 1.20-1.81), use of marijuana (OR: 1.41, 95% CI, 1.15-1.74), and injection drug use (OR: 2.51, 95% CI: 1.57-4.02). Lead exposure was not associated with use of cocaine and methamphetamine.
Conclusions: Lead exposure was significantly associated with increased odds of substance use. Additional research that employs longitudinal data, detailed temporal information, and potential neuropsychological mediating factors should be conducted to rigorously evaluate the role of lead exposure in risk-taking behaviors such as drug use.
Financial Support: None

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HOW DOES CHANGE IN ALCOHOL MISUSE AND DEPRESSION COMORBIDITY IMPACT ON NEUROPSYCHOLOGICAL TEST PERFORMANCE AFTER 12 MONTHS?

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Aims: Alcohol misuse and depression are frequently comorbid and have associated cognitive impairments. This is one of the few studies to focus on the impact of this comorbidity on cognitive function and the long term corollaries of change in depression and/or alcohol misuse. We hypothesized that in people with comorbid depression and alcohol misuse (CAD), a substantial reduction in alcohol use would be associated with improved memory and executive function. Reduction of depressive symptoms was expected to relate to improved verbal memory and verbal fluency. Those who no longer met the study's alcohol and depression entry criteria at 12-months were hypothesized to show improvement in memory and executive function.
Methods: Neuropsychological assessment was administered at baseline and after 12-months to 71 people with a CAD presentation who participated in psychological intervention in the interim. Statistical analyses: Repeated measures ANCOVAs examined the difference between baseline and 12-month scores on neuropsychological tests for those who improved and failed to improve in symptoms of depression and/or alcohol use.
Results: Reducing the frequency and volume of alcohol use was associated with significant improvements in memory, executive functioning, fluid intelligence and intellectual functioning. Improvement in depressive symptoms was reflected in significantly better verbal memory, executive functioning and fluid intelligence. Improvement in both alcohol use and depression was associated with significant improvement in fluid intelligence and visual processing.
Conclusions: We have shown that in a CAD sample significant improvement in cognitive functioning is possible. These results provide evidence for a compelling behavior change message, that by increasing their number of alcohol free days, a client with alcohol misuse can improve their memory, executive functioning and general intellectual functioning.
Financial Support: The National Health and Medical Research Council (Application ID: 351115).
The NSW Health Drug and Alcohol Council Research Grants Program.

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FREQUENCY AND INTENSITY OF CRAVING AMONG ADDICTED PATIENTS DURING OUTPATIENT TREATMENT.

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Aims: Craving is one of the major targets in addiction treatment to maintain abstinence and prevent relapse. However, few studies have examined the evolution of craving during outpatient treatment. This prospective study aimed to describe craving at baseline and after 3 months of treatment.
Methods: Participants were recruited in an outpatient addiction clinic at their treatment entry. Craving data were collected through a questionnaire designed for this study that gathered the frequency of craving in the past 30 days, and average and maximal intensity of craving were assessed within a 10-point visual scale. The characteristics and the severity of addiction were assessed with the Addiction Severity Index (ASI). Data were described at baseline, and ANOVA analyses were used to describe factors associated with baseline craving. Craving at baseline and after 3 months of treatment was compared with Wilcoxon signed-rank test.
Results: Among the 214 patients assessed at baseline (68.3% males, 38.3 y.o.), craving was experienced during 18.3 days on average, with a mean of 6.9 of average intensity and a mean of 8.6 of maximal intensity. Women exhibited higher intensity of craving than men (7.6 vs 6.5; p=.001). The past 30 days frequency of using the main problematic substance was associated with higher craving frequency (p<.0001) and higher average craving intensity (p=.003) past 30 days. Patients with higher severity of addiction had greater frequency (p<.0001) and higher maximal craving intensity (p=.045). Craving was more frequent for tobacco than for alcohol, opiates or behavioral addiction (p<.05). After 3 months in treatment, craving showed a significant decrease in frequency (19.1 days vs 14.5 days, p=.042) and maximal intensity (9.1 vs 8.0; p=.002).
Conclusions: This study offers a better understanding of craving. The significant decrease of craving at 3-month outpatient treatment suggests the continued necessity to focus on this phenomenon for preventing relapse.
Financial Support: PHRC 2006, MILDT 2010, PRA-CNRS-CHU 2008

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A PROCEDURE FOR RAPID DETERMINATION OF DELAY DISCOUNTING OF DRUG AND NON-DRUG REINFORCERS IN MONKEYS.

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Aims: The value of a reinforcer decreases as delay to its delivery increases, a phenomenon referred to as delay discounting and thought to reflect degree of impulsive choice. Previous delay-discounting research with drug and non-drug reinforcers in monkeys has used a procedure that requires at least several months to complete. The present study examined whether orderly delay-discounting functions could be obtained with drug and non-drug reinforcers using a relatively rapid procedure. We hypothesized that choice of a larger reinforcer would decrease with increases in delay to its delivery, regardless of reinforcer type.
Methods: Four male rhesus monkeys chose between smaller, immediate and larger, delayed reinforcers. The delay to the larger reinforcer increased every 3 days until choice switched from the larger to the smaller alternative. Discounting functions were determined for cocaine (0.1 vs 0.025 or 0.2 vs 0.05 mg/kg/inj), remifentanil (0.4 vs 0.1 or 0.8 vs 0.2 μg/kg/inj), and food (4 vs 1 or 8 vs 2 pellets/delivery). Sessions consisted of 8 sample followed by 10 choice trials. Trials were separated by a 20-min inter-trial interval.
Results: For all reinforcer types, choice of the larger, delayed reinforcer decreased as delay to its delivery increased. Individual delay-discounting functions required from 15 to 32 sessions and were orderly and replicable across multiple determinations.
Conclusions: Previous delay-discounting procedures with drug and non-drug reinforcers in monkeys have required a relatively long time to complete, making it difficult to examine whether behavioral or pharmacological manipulations could be used to decrease choices deemed impulsive. The rapid delay-discounting procedure used in this experiment was successful at obtaining orderly discounting functions in a relatively short period of time, making this procedure potentially useful for examining effects of behavioral and pharmacological treatments on delay discounting.
Financial Support: This research was supported by grant R01-DA-027666 to KBF from the National Institute on Drug Abuse.

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BEHAVIORAL INCENTIVES TO PROMOTE EXERCISE COMPLIANCE IN COCAINE-DEPENDENT WOMEN.

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Aims: Low rates of patient compliance have made studying the benefits of regular exercise on women with substance use disorders (SUD) impractical. Contingency management (CM is) strategy for promoting behavior change, which has been successful in reinforcing behaviors such as drug abstinence and treatment attendance. CM offers incentives (prizes) contingent upon target behaviors. Due to expense, CM is often delivered with an escalating variable ratio schedule (Petry et al., 2005). As a Stage Ib behavioral therapies development project (Rounsaville et al., 2001), the primary aim was to test behavioral incentives (BI) to promote regular physical activity in cocaine-dependent women in residential SUD treatment. The target was physical activity, defined as: 30 minutes of treadmill walking (any pace) and treadmill walking (moderate intensity).
Methods: A pilot RCT compared physical activity rates over six weeks in women with Cocaine Dependence randomized to BI (n = 10) or control (C, n = 7) groups. All participants completed baseline assessments, attended a 45-minute health/fitness education class, and were scheduled to exercise three days/week. BI participants were eligible three days/week, to receive incentives for meeting the target behavior(s). Follow-up assessment occurred at 3- and 6-weeks post-randomization, and 4-weeks post-discharge from the residential program. The primary outcome variables (% of sessions completed and total time in sessions) were used for effect size estimations, which were used for power analyses to estimate sample size for Stage II of a RCT.
Results: A significant group effect demonstrated the BI group spent more minutes in scheduled exercise sessions than the C group. Results provide benchmark data on the use of BI to promote physical activity in cocaine-dependent women.
Conclusions: Findings support BI to promote exercise compliance, which can inform development of SUD programs that directly utilize the mental and physical health benefits of physical activity.
Financial Support: Funding from VCU Institute for Women's Health, NIH National Institute for Drug Abuse, (R36DA30619-2,) and the NIDA Clinical Trials Network (CTN).

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MODEL MINORITY STEREOTYPE, PSYCHOLOGICAL DISTRESS,SUBSTANCE USE AMONG ASIAN-AMERICAN YOUNG ADULTS.

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Aims: Risk behaviors including substance use, are a growing problem among U.S.-born Asian American young adults, however, the determinants underlying this trend are poorly understood. One distinct factor for U.S.-born Asian Americans that may increase risk behavior is the endorsement of the "model minority" stereotype. Based on the negative affect regulation theory endorsing the "positive" stereotype of the model minority (i.e., the belief that all Asians are high academic achievers and financially well-off) may heighten psychological distress and, in turn, confer risk for problem drinking. The aim of this study is to examine the role of the endorsement of the model minority stereotype, psychological distress, illicit drug use (e.g., marijuana use, non-prescription drugs) and alcohol-related problems among Asian American young adults.
Methods: Participants included 162 U.S-born Asian American young adults recruited from the Maryland and Washington, DC area. Participants completed a measure of endorsement of the model minority stereotype(two subscales:1) achievement orientation or the myth that Asian American's success is due to stronger work ethic and drive for success, and 2)unrestricted mobility or the myth that this group experiences less perceived racism and barriers at work), psychological distress and substance use.
Results: Rates of alcohol-related problems and illicit drug use appear to be higher in the current sample, compared to previous studies. Structural equation modeling results suggest that the two model minority stereotype scales had an indirect effect on alcohol-related problems and illicit drug use through psychological distress and heavy episodic drinking.
Conclusions: Asian American young adults are increasingly becoming an at-risk group for risk behaviors including alcohol-related problems and illicit drug use. Endorsing the "positive" model minority stereotype appears to be a risk factor for alcohol related problems and illicit drug use by heightening psychological distress, which supports the negative affect regulation framework.
Financial Support: R03DA03267601A1

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DETECTION OF OPIOID OVERDOSES AND POISONINGS IN ELECTRONIC MEDICAL RECORDS AS COMPARED TO MEDICAL CHART REVIEWS.

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Aims: The study assessed the proportion of opioid overdose and poisoning (OOP) events identified by ICD diagnostic codes in electronic medical records that were true OOP events as confirmed by medical chart review (ie, the positive predictive value of ICD codes). Accurate identification of OOP events is essential if data are to be used to assess population risk, care quality, or evaluate preventive interventions.
Methods: The study population consisted of the Kaiser Permanente Northwest and Northern California memberships between August 2008 and October 2012. ICD diagnostic codes possibly indicative of overdoses were selected from published literature and putatively related ICD codes. Events identified from codes were compared to medical chart outcomes. All overdoses were included, regardless of opioid prescriptions or pain diagnosis. Two groups of opioid-specific ICD codes were assessed: 1) adverse event codes (E935.x and Y45) combined with ICD codes for overdose symptoms (eg, altered consciousness, respiratory distress, etc.) and 2) poisoning codes (965.xx, E850.x, and X42).
Results: Adverse event codes were not predictive of OOP events: only 13% were confirmed as OOP events by chart review. Poisoning codes were more predictive. Of 2,045 opioid poisoning events identified by ICD codes, 382 (18.7%) had no medical chart entry and were excluded from the study. Of the remaining 1,663 OOP events, 64.3% (1,070) were confirmed opioid analgesic-related overdose/poisonings (44.7% unintentional and 19.7% intentional), 14.1 % (235) were OOP events associated with opioid anesthesia, 16.5% (274) were opioid adverse events but not overdose/poisonings, 4.0% (67) were miscoded, 0.5% (7) were misidentified, and 0.5% (7) were missing data.
Conclusions: The ICD codes for opioid-related poisoning had a positive predictive value of 64.3% to detect opioid overdose/poisoning events not related to inpatient opioid anesthesia, and increases to 78.5% if analgesic-related overdose/poisonings are included.
Financial Support: Purdue Pharma

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ESTIMATED EFFECT OF STATE SYRINGE POLICY ON SOURCE OF LAST-USED INJECTION EQUIPMENT.

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Aims: Many injection drug users (IDUs) share or re-use injection equipment, leading to elevated infection risk (e.g., HIV; HCV). Via nationally representative sample survey data from states with contrasting syringe policies, we estimate cross-state differences in the source of IDU's last-used syringe.
Methods: Data are from National Surveys on Drug Use & Health (RDAS, 2002-2009), with n=994 active IDUs identified via IRB-approved computerized self-interviews. The RWJ Foundation LawAtlas(SM) sorted states by syringe policy (e.g., requiring a prescription). Weighted estimates with Taylor series variances are reported.
Results: As hypothesized, when IDUs reside where state policy discourages pharmacy syringe acquisition, last-used syringes more likely come from unsafe sources (e.g., shooting gallery). Among IDUs in less restrictive states (vs those with restrictive policies), last-used syringes were more likely from safe sources: pharmacy or needle exchange program (overall difference, D = 12%; 95% CI = 3%, 22%; $p < 0.05$). Nationwide, pharmacies predominate as most likely sources for last-used syringes: for IDUs in less restricted states, 64%; for those in other states, 42% (difference, D = 22%; 95% CI = 12%, 31%; $p < 0.05$). These variations have little to do with the drug being injected; variations with race-ethnicity can also be seen.
Conclusions: An unintended negative health behavior externality may arise where IDUs face state policies that discourage syringe acquisition from pharmacies — namely, greater acquisition from unsafe sources, even where needle exchange programs are financed to offset pharmacy restrictions. IDUs residing in less restrictive states are more likely to have obtained the last-used syringe from a safe source. Within syringe-restrictive states, where there are areas of IDU density, area-randomized syringe policy variations might be structured to yield experimental evidence about both intended and unintended effects of syringe restrictions (in terms of IDU behavior, health, and health care costs).
Financial Support: NIDA T32DA021129 (PJ); K05DA015799 (JCA).

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RACIAL AND ETHNIC DISPARITIES IN SUBSTANCE USE AND OUTCOMES IN ELDERLY PROSTATE CANCER PATIENTS.

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Aims: To analyze racial disparity in substance use prevalence and outcomes in elderly Medicare patients with advanced prostate cancer.
Methods: Linked database of SEER-Medicare was used to extract a cohort of elderly men diagnosed with advanced prostate cancer between 2001 and 2004, and also having a claim for substance use (ICD-9 codes: Alcohol dependence syndrome-303.xx, Drug dependence 304.xx and Non-dependent abuse of drugs 305.xx). We compared health service use, cost and mortality across three racial and ethnic groups.
Results: Our cohort consisted of 14,277 elderly with advanced prostate cancer. Substance use prevalence was highest for African Americans (16%), compared to Whites (10%) and Hispanics (9%). Comparison within each racial and ethnic group showed that those with substance use had consistently higher health service use, cost and mortality. Comparison between racial and ethnic groups indicated significant variation in health service use, cost and mortality. Mortality was highest for African Americans, compared to White and Hispanic (57% vs. 45% and 50%, respectively). On the other hand, though Hispanics had the lowest prevalence of substance use, in the one year period following diagnosis of prostate cancer, they had highest ER use (28%), compared to Whites (23%) and African American s(19%). Whites had the highest inpatient use and outpatient use (74% and 86%, respectively) and highest costs.
Conclusions: While racial and ethnic variation in outcomes among prostate cancer patients ware well documented, the presence of substance use appears to further exacerbate these disparities. This emphasizes the need for interventions to address substance use among elderly prostate cancer patients that are sensitive to the racial and ethnic variation.
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PROCESS EVALUATION OF A COMMUNITY COLLABORATIVE BOARD: USING COMMUNITY-BASED PARTICIPATORY RESEARCH TO CREATE A SUBSTANCE ABUSE/ HEALTH INTERVENTION.

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Aims: To evaluate the structure and dynamic process of a CCB whose goal was to create an evidence-based substance abuse/ health intervention for ex-offenders and to provide lessons learned to enhance future CBPR endeavors.
Methods: Meeting notes, attendance, video recordings, and in-depth interviews with 13 CCB members at baseline (Baseline: two weeks after the CCB's first meeting) and eleven members at twelve months follow-up were used to conduct an independent process evaluation. Open coding identified themes and patterns across answers regarding membership engagement, retention, and power distribution.
Results: Results showed member retention (73.3% retention rate) was due to strong personal commitment to the targeted problem. Analysis also revealed an unequal power distribution between members. Nevertheless, the development of an innovative, community-based health intervention manual was accomplished within one year. Aspects of the process, such as, incentives, sub-committees and trainings, enhanced the Board's ability to integrate the community and scientific knowledge to accomplish its research agenda.
Conclusions: CBPR was a useful framework in enhancing quality and efficiency in the development of an innovative, community-based substance abuse/ health intervention manual for distressed communities. The use of a structured format, incentives, sub-committees, and trainings proved critical in the success of this process. Overall, this article sheds light on a process that illustrates the integration of community-based and scientific knowledge to address the health, economic and societal marginalization of low-income, minority communities.
Financial Support: The study was supported by Award Number P30MH079920 from the National Institute of Mental Health. The authors were supported as postdoctoral and pre-doctoral fellows in the Behavioral Sciences Training in Drug Abuse Research Program sponsored by Public Health Solutions and National Development and Research Institutes with funding from the National Institute on Drug Abuse (5T32DA007233).

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CONNECTING STATES AND TRAITS: A LOOK AT PERSONALITY AND RESPONSE TO STRESS IN REAL-TIME.

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Aims: Personality traits may help predict perceptions of and responses to stressors. In substance misusers, these are likely to influence relapse and recovery. Here we looked at the relationship between Big Five personality traits and real-time self reports (Ecological Momentary Assessment, EMA) of mood and perceived stressful events in substance users.
Methods: Methadone-maintained drug users (n=94) reported moods and stress in real time via EMA for 16 weeks in random prompts (RP) and self-initiated reports of stress. In week 3, participants completed the 60-item NEO-FFI supplemented with 6 items from the NEO-PI (to assess Vulnerability to Stress (VS; one facet of Neuroticism; N)). Multilevel models (SAS Proc Mixed and Proc Glimmix) were used to assess NEO percentile scores as predictors of the contents of momentary self-reports.
Results: Compared to published norms, our cohort scored below population median on all traits except N and VS; mean percentile scores: N 55; Extraversion (E) 46; Openness (O) 38; Agreeableness (A) 41; Conscientiousness (C) 44; VS 54. In self-initiated reports of stress, NEO scores differentially predicted reports of specific stressors. VS predicted greater likelihood of having been stressed by feeling one's surroundings were unsafe; A and C predicted greater likelihood of having been stressed by interpersonal conflict. High scores on N (or O) predicted greater likelihood of having been stressed by simply thinking about stressful things. In RP entries, VS predicted greater scores on momentary negative mood, and A predicted greater scores on momentary positive mood.
Conclusions: These results show how momentary mood and stress responses may differ as a function of specific traits. Results from trait analysis could be useful in predicting types of stress most bothersome to specific personality types, and potentially predict likely responses. Combining information from personality traits and real-time assessments may facilitate implementation of real-time personalized treatment strategies.
Financial Support: This work was supported by the Intramural Research Program of NIDA, NIH.

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DOPAMINE D2/D3 RECEPTOR MODULATION OF FOOD-DRUG CHOICE IN RHESUS MONKEYS.

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Aims: Within the dopaminergic system, the dopamine D3 receptor (D3R) has been shown to mediate many of the behavioral effects of psychostimulants associated with high abuse potential. Recent preclinical studies have shown that buspirone (Buspar®), a D3/D2R antagonist, was able to decrease cocaine self-administration in rhesus monkeys responding under multiple schedules of cocaine and food reinforcement. Thus, the present study sought to extend the assessment of buspirone on cocaine and methamphetamine (MA) self-administration and reinstatement to include a food-drug choice procedure. These effects were compared with the non-selective D2-like receptor antagonist eticlopride and the highly selective D3R antagonist PG01037.
Methods: Seven male rhesus monkeys served as subjects in which complete cocaine and MA dose-response curves were determined daily in each session. Buspirone (0.01-0.3 mg/kg, i.m.) and eticlopride (0.001-0.01 mg/kg, i.v.) were administered chronically (5 days) to monkeys self-administering cocaine and MA (n=3/group) while PG01037 (1.0-5.6 mg/kg, i.v.) was administered acutely (n=4). The ability of buspirone (1.0-1.7 mg/kg, p.o.) to block reinstatement was examined using the choice procedure in which saline was substituted for the self-administered drug (n=3/group).
Results: Neither buspirone nor eticlopride decreased drug choice or intake while buspirone significantly increased the choice of low drug doses. However, buspirone attenuated both cocaine- and MA-induced reinstatement. Further, PG01037 was effective in reallocating choice behavior from cocaine to food responding in 2 of 4 monkeys.
Conclusions: These data support a potential use for buspirone in the drug abuse treatment of relapse and support the continued examination of D3 compounds for novel therapeutic agents.
Financial Support: DA012460, NIDA-IRP

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MARIJUANA USE AMONG LOW-INCOME URBAN YOUTH: A SYSTEMATIC REVIEW.

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Aims: To assess whether adolescents in low-income, urban areas are less likely to use marijuana as compared to the general population of adolescents.
Methods: We systematically reviewed articles from 1997-2012, that focused on US youth aged 12-18 in urban areas. Samples of youth who were incarcerated, in substance abuse treatment, or homeless were excluded.
Results: We identified 39 unique articles that met review criteria. Just 10.3% of the articles focused specifically on marijuana use, whereas 51.3% considered marijuana along with other substances. The final 38.5% reported marijuana use prevalence, though marijuana was not a major focus of the study. More than half (53.8%) of the studies conducted analysis using cross-sectional data, 41% used longitudinal data, and 2% used other methods or a combination of both cross-sectional and longitudinal data. Methods researchers used to assess marijuana use varied greatly. Of the 39 articles identified, 14 studies requested adolescents to report past 30-day marijuana use. Researchers recruited the majority of the participants in the selected studies in school settings (53.8%) and primarily included racial and ethnic minorities. Clinical based urban samples tended to report higher use of marijuana than school based samples, but this was not consistent or could not be comparatively determined due to variation in data collection methods.
Conclusions: Overall, populations of urban adolescents report marijuana use at levels similar to the general population. There is still much to be understood about marijuana prevalence among urban adolescents; contextual geographical and community differences may impact marijuana prevalence more than other indicators.
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EFFECTS OF TRAINING AND IMPLEMENTATION EXPERIENCE ON CLINICAL SKILLS INVOLVED IN DELIVERING CONTINGENCY MANAGEMENT.

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Aims: Contingency Management (CM) is efficacious in addiction treatment and requires clinicians to perform a variety of skills during client contacts. While there is data to suggest that training improves overall CM delivery skills, little is known about how training may differentially impact specific skill areas, and what skill areas merit greater emphasis in training. This study reports the effects of training and 90 days of CM implementation experience on the delivery skills of clinicians working at a community based opiate treatment program.
Methods: Staff (N=16) participated in a 16-hour training workshop, dispersed as four weekly half-day sessions at their clinic, and completed standardized patient (SP) intervention assessments one week prior, one week following training, and at a follow-up assessment after a 90-day period of trial implementation. Two sets of repeated-measures analysis of variance (RM-ANOVA) were conducted. The first, focused on immediate training impacts, assessed temporal change in CM skill areas from pre- to post-training. The second, focused on eventual impact of training and implementation experience, assessed temporal change from pre-training to follow-up. Given the sample size, corresponding sets of Cohen's D for dependent measures were also computed.
Results: Across individual skill areas, RM-ANOVA were statistically significant ($p < .01$). All of the immediate training effects were robust ($d = .76 – 2.49$), as were eventual effects of training + implementation ($d = .89 – 2.63$). Interestingly, eventual effect sizes were greater for 4 of the 6 skill areas, suggesting additive effects of training and implementation experience.
Conclusions: Findings indicate robust, durable effects of training on CM delivery that are evident at the 90-day follow-up. Furthermore, it appears that the clinicians had greater improvement of CM delivery at follow-up indicating the potential that experience aided in clinician's ability to deliver CM. However, this was not uniform over all skill areas.
Financial Support: K23 DA025678

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ADOLESCENT ATTACHMENT AND SUBSTANCE USE: CONCURRENT AND PROSPECTIVE LINKS.

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Aims: Prior research supports a link between attachment (i.e., patterns of thoughts, feelings, and behaviors in close relationships) and substance use (e.g., Cooper et al., 1998). However, most of this research has been conducted with adults or with clinical samples. Therefore, the aim of this study was to examine the concurrent and prospective links between attachment and substance use in a community sample of adolescents. We predicted that adolescents reporting greater attachment anxiety would be more likely to report using substances, whereas adolescents reporting greater attachment avoidance would be less likely to report using substances.
Methods: The sample included 207 adolescents (M = 15.04 years, SD = .95; 51% Caucasian; 44% female) assessed at two time points over a period of 1 year. We measured two dimensions of attachment (avoidance and anxiety) with the well-validated Experiences in Close Relationships Scale (Brennan et al., 1998). We measured past year alcohol and marijuana use and binge drinking using the Youth Risk Behavior Surveillance System (CDC, 2002).
Results: Logistic regression analyses with concurrent data revealed that adolescents reporting greater attachment anxiety were more likely to consume alcohol in the past year at both assessments (Time 1, OR: 2.30, $p < .001$; Time 2, OR: 2.35, $p < .001$), and to report engaging in binge drinking at Time 2 (OR: 1.67, $p < .05$), after adjusting for age, gender, ethnicity, and family income. Prospective analyses revealed that adolescents reporting greater attachment anxiety at Time 1 were more likely to report consuming alcohol at Time 2 (OR: 1.91, $p < .01$), whereas adolescents reporting greater attachment avoidance were less likely to report consuming alcohol at Time 2 (OR: 0.67, $p < .05$), after adjusting for covariates. No significant findings emerged in relation to marijuana use.
Conclusions: Attachment is related to the likelihood and severity of alcohol use, but not marijuana use, in a community sample of adolescents. Future research should aim to identify mediators and moderators of these links.
Financial Support: NIDA R01DA018647; F31DA033848

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THE EFFECTS OF PIOGLITAZONE, A PPARγ RECEPTOR AGONIST, ON THE ABUSE LIABILITY OF OXYCODONE.

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Aims: Activation of glial cells by opioids is thought to play an important role in opioid-induced reward, tolerance, and dependence. Preclinical research has shown that the glial inhibitor pioglitazone (PIO) is capable of preventing the acquisition of heroin self-administration, and reducing stress-induced reinstatement of heroin seeking. The ability of PIO to alter the effects of opioids in humans has not been characterized in a controlled, laboratory setting. Accordingly, the proposed investigation seeks to examine the effects of PIO on the subjective effects of oxycodone.
Methods: Prescription opioid abusers who were not physically dependent on opioids were maintained on ascending daily doses of PIO (2-3 weeks on placebo, 2-3 weeks on 15 mg, 2-3 weeks on 45 mg). Following at least 14 days of maintenance on each PIO dose, a laboratory session occurred during which the subjective effects of oxycodone were characterized using a cumulative dosing procedure (0, 10, and 20 mg, cumulative dose = 30 mg).
Results: Data from 15 participants who completed the study were available at the time of this analysis. Oxycodone produced dose-dependent increases in positive subjective responses. Overall, ratings such as: drug "liking," "high," and "good drug effect," were not significantly altered as a function of PIO maintenance dose. PIO also did not affect oxycodone-induced ratings of "Bad" drug effect, which were generally minimal (<10 mm on a VAS between 0 and 100 mm). On its own, PIO appeared to have no positive or negative subjective effects.
Conclusions: These data suggest that PIO does not alter the positive or aversive effects of moderate doses of oxycodone, and therefore has little impact on the drug's abuse liability. Although PIO failed to alter the abuse liability of oxycodone, the interaction between glia and opioid receptors is not well understood so the possibility remains that medications that interact with glia in other ways may show more promise.
Financial Support: NIDA grant R01DA031022 to SDC and K01DA030446 to JDJ

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MORPHINE AND INTERLEUKIN-1 RECEPTOR ANTAGONIST PREVENT THE DEVELOPMENT OF STRESS-ENHANCED FEAR LEARNING.

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Aims: Post-traumatic stress disorder (PTSD) is a pathological condition in which a severe trauma produces debilitating psychological and physiological consequences. Recently, morphine treatment after a trauma has been associated with reduced rates of PTSD. We have translated this effect to an animal model of the disorder, stress-enhanced fear learning (SEFL). However, morphine's high abuse liability severely limits its use as a potential preventive treatment for PTSD. Here, we test the hypothesis that neural cytokines are a key mechanism of morphine's action in preventing SEFL.
Methods: In experiment 1, rats (N=36) were exposed to the severe stressor of the SEFL paradigm, and were sacrificed immediately, 6, 24, 48, or 72h later. A control group was exposed to the context without footshocks. Brain sections were stained with primary antibodies against interleukin-1β (IL-1β). Alexa Fluor 488 conjugated secondary antibodies were used for visualization. Total plasma corticosterone (CORT) was measured by radioimmunoassay. In experiment 2, rats (N=43) were implanted with intracerebroventricular cannulae and subjected to the SEFL paradigm. At 24 and 48 hours after severe stressor, animals were administered either saline vehicle or 10μg of IL-1 receptor antagonist (IL-1Ra).
Results: In experiment 1, IL-1β was enhanced in the dorsal hippocampus at 6 through 72h. As expected, plasma CORT was significantly elevated immediately ($p<.05$) after the stressor and returned to baseline at 6h. Interestingly, CORT was re-elevated at 48 ($p<.05$) and 72h ($p<.05$) after the stressor. In experiment 2, IL-1Ra administration significantly attenuated fear learning to a subsequent single shock ($p<.05$), i.e. prevented stress-enhanced fear learning.
Conclusions: These results lend support to the hypothesis that IL-1β may be a target of morphine's action and, therefore, may be a potential target for PTSD treatment with less abuse potential than morphine.
Financial Support: T32-DA07244-21-25

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ADOLESCENT ATOMOXETINE, BUT NOT METHYLPHENIDATE, DECREASES COCAINE-SEEKING BEHAVIOR IN A GENETIC MODEL OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

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Aims: Attention-deficit/hyperactivity disorder (ADHD) is often comorbid with cocaine abuse. Controversy exists regarding long-term consequences of ADHD medication use on cocaine abuse risk. In rodents, adolescent methylphenidate (MPH) treatment increases adult cocaine self-administration in the Spontaneously Hypertensive Rat (SHR) genetic model of ADHD, whereas adolescent atomoxetine (ATO) treatment does not. Effects of ADHD medications on cocaine cue reactivity, a critical component of addiction, are unknown. We hypothesized that adolescent MPH and ATO would alter cocaine intake and cue reactivity differently in adult SHR.
Methods: SHR, Wistar-Kyoto (inbred control) and Wistar (outbred control) strains, received MPH (1.5 mg/kg, p.o.), ATO (0.3 mg/kg, i.p.), or their respective vehicles from P28-P55 (n=7-10/strain and treatment). Cocaine seeking, which reflects cue reactivity, was measured in adulthood during self-administration maintenance and cue-induced reinstatement conducted under a second-order schedule.
Results: Compared to control strains, adult SHR earned more cocaine infusions, emitted more cocaine-seeking responses during maintenance and reinstatement testing, and required more sessions to reach the extinction criterion ($ps \leq 0.05$). Compared to vehicle, adolescent MPH, but not ATO, increased cocaine intake during maintenance testing in adult SHR ($p \leq 0.01$). Adolescent ATO, but not MPH, decreased cocaine seeking during reinstatement testing in adult SHR ($p \leq 0.03$). Neither medication had effects on cocaine intake or cue reactivity in control strains.
Conclusions: This research further supports ADHD and cocaine abuse comorbidity and shows differential effects of ADHD medications on cocaine abuse risk in SHR. Thus, SHR have heuristic value for assessing the neurobiology underlying the ADHD phenotype and the evaluation of pharmacotherapeutics for ADHD.
Financial Support: DA011716

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ADOLESCENTS ARE DRIVEN BY INCENTIVE VALENCE, NOT MAGNITUDE, ON THE MONETARY INCENTIVE DELAY TASK.

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Aims: Initial onset of substance use occurs most often during adolescence, which is a particularly vulnerable period that may set the stage for subsequent substance abuse problems. Vulnerability to substance abuse may be attributed to stronger reward-driven motivation systems in adolescents, but this issue is debated. The goal of this study was to examine neural correlates of incentivized motivation in adolescents and adults using the monetary incentive delay (MID) task. This study tests the hypothesis that adolescents are driven more by reward prospects and outcomes (i.e., positive valence) than adults.
Methods: 20 adolescents (11-14 years) and 49 adults (18-25 years) completed an fMRI MID task using 5 incentive values (-$5, -.5, 0, .5, 5) that varied in valence (positive, negative) and magnitude (high, low). fMRI signal in the cue and feedback phases of the MID was examined using ANOVAs, and incentive functions in adults and adolescents were further examined to determine whether they best fit a linear or quadratic function. A better linear than quadratic fit indicates greater sensitivity to incentive valence, but a better quadratic fit indicates greater sensitivity to incentive magnitude.
Results: In the bilateral nucleus acumbens (NAc), cue-phase incentive functions in adults showed greater sensitivity to high values, regardless of valence (i.e,. magnitive sensitivity), but in the right NAc in adolescents, there was greater sensitivity to positive vales (i.e., valence sensitivity). In the bilateral caudate nucleus, feedback-phase incentive functions in adults showed greater sensitivity to small values, regardless of valence, but in adolescents these regions showed trends toward greater sensitivity to negative values.
Conclusions: Although adolescents show more reward sensitivity during the cue phase of the MID, they showed more loss sensitivity in the feedback stage. Additional analyses will explore the association of these profiles with impulsivity and sensation seeking personality traits.
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TEEN GIRLS AND BOYS OF TREATED SUBSTANCE-ABUSING MOTHERS.

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Aims: Maternal substance abuse and mental illness can adversely impact child development. We examine if teen boys and girls are differentially influenced by maternal problems.
Methods: Mothers of the youth (88 girls, 101 boys; age range: 10-17) were recruited at admission to 44 treatment programs in 13 California counties during 2000-2002. Addiction severity index (ASI) was administered at both intake and follow-up in 2010-2011. Child functioning data were reported by mothers using the Child Behavior Checklist (CBCL). Separate multiple regression analysis was conducted for internalizing (anxiety/depression, social withdrawal, somatic complaints) and externalizing (thoughts problem, attention problem, aggressive behavior) problems, and the multiple-group approach was used to test the difference on maternal influences between girls and boys.
Results: Girls and boys did not differ in syndromes or problem scales on the CBCL. Results based on the multiple regression analysis using the multiple-group approach show that maternal ASI drug use severity was significantly associated with social withdrawal ($\beta = 7.7$ for girls vs. $\beta = -1.1$ for boys) and aggressive behaviors (18.1 vs. -3.4) among girls but not among boys; maternal ASI psychiatric severity was associated with social withdrawal (-0.3 vs. 3.8), thoughts (0.8 vs. 3.9) and attention (-0.1 vs. 7.7) problems for boys but not for girls—although maternal psychiatric problem was significantly associated with somatic complaints for both girls and boys; and maternal family problem severity was significantly related to girls' social withdrawal and boys' thoughts problems.
Conclusions: Despite similar levels of syndromes or problem severity, girls and boys of substance-abusing mothers are influenced by different aspects of maternal conditions; maternal substance use may particularly confer risk for girls' problem behaviors.
Financial Support: None

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VARENICLINE IMPROVES INFORMATION PROCESSING SPEED AND VERBAL MEMORY IN METHAMPHETAMINE-DEPENDENT PARTICIPANTS.

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Aims: Evaluate whether short-term treatment with varenicline improved neurocognition in non-treatment seeking methamphetamine (METH)-dependent volunteers. We hypothesized that varenicline would improve neurocognition.
Methods: This double blind, placebo-controlled, within-subjects trial of varenicline evaluated neurocognition in 17 volunteers. Participants were randomly assigned to receive one dose of oral varenicline (0, 1, or 2 mg) during three separate inpatient phases. Neurocognition, assessed prior to and after 5 days treatment with each dose, included the Continuous Performance Task-II, N-Back, Hopkins Verbal Learning Task–Revised, and the Wechsler Adult Intelligence Scale–III.
Results: The sample was primarily Caucasian (71%), male (71%), and ~36 years old. On average, participants used ~1 gram of METH/day, ~13 days out of the last 30 days, for ~14 years. When considering all 3 phases, no medication effects were detected by repeated measures ANOVA. In contrast, when considering the 2 active treatment phases, participants demonstrating relatively slow information processing speed on the n-back and relatively poor verbal memory at baseline (defined using a median split of the mean of the 3 baseline assessments, thus 6-8 subjects were lower performers in each group), showed significantly faster reaction times on the n-back for both visual ($F(2,6)=7.642$, $p=0.022$, $\mu 2=0.718$) and auditory ($F(2,6)=9.427$, $p=0.014$, $\mu 2=0.759$) stimuli. In addition, there was a trend where varenicline improved recall on the learning trials of the HVLT-R ($F(2,5)=4.403$, $p=0.079$, $\mu 2= 0.638$) and the effect size was very large.
Conclusions: This is the first study to show that varenicline increased information processing speed and improved verbal memory in METH-dependent individuals. Because of the small sample size and short dosing time-frame, these findings need to be replicated in a larger sample over a longer period of time.
Financial Support: This work was conducted at, and supported by the Michael E. DeBakey VA Medical Center, Houston, TX. Funding from NIH to RDLG: DA 027134.

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MODAFINIL AND NALTREXONE FOR THE TREATMENT OF COMORBID COCAINE AND ALCOHOL DEPENDENCE.

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Aims: The co-occurrence of cocaine and alcohol dependence is very common and difficult to treat This clinical trial was intended to evaluate the efficacy of naltrexone and modafinil for the treatment of comorbid cocaine and alcohol dependence. Naltrexone, a mu opiate receptor antagonist, has been shown to reduce heavy drinking in alcoholics. Recently, we found that high-dose naltrexone may have efficacy for reducing relapse to cocaine and alcohol in dually addicted cocaine and alcohol dependent patients. Modafinil has both dopaminergic and glutamatergic activity that could be useful for the treatment of cocaine dependence. Modafinil was found to block the euphoric effects of cocaine in three independent human laboratory studies and has also been shown to reduce cocaine use in several clinical trials. In this trial, the efficacy of naltrexone and modafinil individually and in combination was evaluated.
Methods: The study was a double-blind, placebo-controlled, trial involving 164 DSM-IV alcohol and cocaine dependent subjects. Subjects were randomized into 4 groups: modafinil 400 mg. daily, naltrexone 150 mg. daily for men or 100 mg. daily in women, the combination of modafinil 400 mg. daily and naltrexone (150 mg. daily for men 100 mg. daily for women), or placebo. Patient received study medication for 13 weeks along with weekly individual therapy. Primary outcome measures included alcohol use, measured by the timeline follow back, and cocaine use, measured by self-report and verified by thrice weekly urine drug screens.
Results: Ninety subjects completed the trial. There was no difference between the 4 groups in treatment retention. Preliminary analyses revealed that none of the three active medication groups was superior to placebo in reducing drinking or cocaine use in this sample.
Conclusions: Modafinil either alone or combined with naltrexone is not efficacious for the treatment of comorbid cocaine and alcohol dependence. Oral naltrexone is not efficacious for the treatment of comorbid cocaine and alcohol dependence.
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ALCOHOL USE AMONG TRAUMATIZED YOUTH IN ZAMBIA.

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Aims: Alcohol use in childhood and adolescence has been associated with a range of psychosocial problems and has also been established as a common trauma outcome. Less is known about the prevalence and correlates of alcohol use among youth exposed to trauma and with co-occurring mental health problems in sub-Saharan Africa. This study assessed the prevalence of alcohol use and its association with trauma exposure among 255 youth (ages 5-18) with significant mental health problems in Zambia.
Methods: Data were utilized from a randomized controlled trial of a mental health intervention. Alcohol use was measured with the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). A trauma type exposure score was calculated with items from the Post-traumatic Stress Disorder Reaction Index (PTSD-RI).
Results: Preliminary cross-sectional analyses at baseline indicated that 28.6% of children reported lifetime use of alcohol, 50% of whom reported drinking in the past 3 months. Boys ($p<.01$) and older children ($p<.0001$) had increased odds of reporting lifetime use. Number of experienced trauma types was associated with drinking in the past 3 months ($p<.01$). Among those who used alcohol in the past 3 months, 34.2% reported functioning problems associated with their drinking and 51.3% reported that they had tried but failed to cut down on their drinking. Longitudinal data from a 12-month follow-up assessing the association of baseline alcohol use with additional trauma exposure will also be presented.
Conclusions: Discussion of the findings will focus on the risk and protective correlates for alcohol use and the implications for intervention strategies among children affected by trauma in Zambia.
Financial Support: This study was made possible with support from USAID (PI: Murray; FS11-GHS-A-00-09-00004.3). Mr. Kane is supported by a NIDA training grant in Drug Dependence Epidemiology (PI: Furr-Holden; T32DA007292). Dr. Michalopoulos is supported by the NIMH HIV Intervention Science Training Program (MH080665).

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NONMEDICAL USE OF OXYCODONE AND OTHER OPIATE ANALGESICS IN THE US, 2004-2011: ARE MILITARY VETERANS AT INCREASED RISK?

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Aims: Alarming increases in opioid prescription misuse have been reported in both veterans and civilians. However, most studies of veterans are derived from VA patients. We compared risks of nonmedical use of oxycodone and other opiate analgesics between veterans and their civilian counterparts, along with major risk factors, over 8 years.
Methods: We utilized samples of veterans and nonveterans matched for age group, gender and race (1:2 ratios) from the National Survey on Drug Use and Health, 2004 to 2011 (subsamples N=56,463). Measures included socio-economic factors, insurance, depression, nonmedical oxycodone and non-oxycodone analgesics use and access, heroin use, and lifetime marijuana, alcohol or nicotine dependence. Estimates were weighted and adjusted for variances using SUDAAN.
Results: Past-year nonmedical oxycodone use among veterans, ranging from 0.16 to 0.58%, was lower than nonveteran counterparts in all years except 2006 and 2008; non-medical use of other opiate analgesics, ranging from 1.47 to 3.08%, was also lower among veterans in all years. Differences were significant for non-oxycodone analgesic misuse only for 2007 (veteran OR=0.61) and 2011 (veteran OR= 0.45). Among users, obtaining oxycodone from relatives/friends for whom a doctor had prescribed use (secondary iatrogenic) was more common among veterans than nonveterans. Multivariate analyses showed that each of the three substance dependence diagnoses was significantly associated with both oxycodone and non-oxycodone use for both samples. Ever heroin use was an exceptionally important risk factor of past-year oxycodone use for both samples (veteran OR=11.99; nonveteran OR=13.60).
Conclusions: Veterans were generally at lower-risk of nonmedical use of opiate analgesics. No significant increases in recent years were detected among veterans. Risk factors were similar between veterans and nonveterans with a strong association of lifetime heroin use for oxycodone misuse.
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EXPLORING NORMATIVE WORKING MEMORY VARIANCE TO BETTER UNDERSTAND DISPARITIES IN RISK FOR DRUG USE DISORDERS.

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Aims: Working memory (WM) plays a central role in goal-directed cognition (i.e. planning, reasoning, learning), and WM deficits represent cognitive vulnerabilities that predispose individuals to drug use and other disorders. The n-back task is arguably the most widely used paradigm for studying the neural basis of WM; however, its neuropsychometric properties as a WM demand remain controversial. We merged clinical neuropsychology and fMRI to (1) investigate the construct validity of a letter (verbal) variant of the n-back (LNB) task and to (2) characterize individual differences in the neural correlates of normative WM function.
Methods: LNB construct validity was assessed using bootstrapped correlations between LNB performance and neuropsychological measures of WM, and measures of unrelated cognitive constructs (i.e. attention, vigilance), to confirm convergent and discriminant validity, respectively. Independent component analysis (ICA) identified brain networks active during the LNB in 35 healthy adults. General linear modeling was used to correlate each network's level of engagement with task conditions to determine WM-specific recruitment.
Results: Correlations revealed convergence between LNB and WM tasks (bootstrapped $|\rho| \geq 0.39$) and divergence from non-WM tasks (bootstrapped $|\rho| \leq 0.33$). ICA identified 35 networks, with 18 showing task-specific engagement. Of these, bilateral frontoparietal, DLPFC, and superior parietal, and frontoinsular networks were preferentially recruited by 2-back vs. 0-back (control) conditions, indicating WM involvement.
Conclusions: These results support the use of the LNB as a WM measure and probe of normative variance in WM performance, as well as a probe of the roles of neural processing networks in the encoding of individual differences in WM and risk for drug use and other disorders.
Financial Support: 8KL2TR000063, 8UL1TR000039, 5R25GM0832, T32DA022981

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EXPERIENCES OF DISCRIMINATION AND PSYCHOSOCIAL HEALTH PROBLEMS AS CORRELATES OF RECENT PRESCRIPTION DRUG MISUSE AMONG YMSM: EVIDENCE OF A SYNDEMIC EFFECT.

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Aims: Prescription drug misuse is a growing public health concern among young adults – including young men who have sex with men (YMSM). While experiences of discrimination (homophobia, racism) have been found to contribute to illicit drug use among YMSM, there is limited knowledge on how these and mental health problems (e.g. stress, depression, anxiety) are associated with patterns of prescription drug misuse (opioids, tranquilizers, stimulants, etc.) in this population. Here, we evaluate whether experiences of discrimination and mental health problems fit into a syndemic framework, and have an additive effect on prescription drug misuse among YMSM.
Methods: A sample of 191 YMSM recruited in Philadelphia reported on experiences of discrimination, mental health problems, and recent (6 months) prescription drug misuse. To test for the additive effect of the syndemic, a logistic regression model was used with syndemic as the independent variable and levels of prescription drugs misuse as dependent variables. High misuse was defined as a misuse of prescription drug class above median; polydrug use was defined as misuse of ≥ 2 classes of prescription drugs.
Results: Psychosocial health problems and experiences of discrimination were highly intercorrelated. In bivariate analyses, all syndemic problems were positively related to high misuse of prescription opioids (except homophobia), tranquilizers, and other pills (muscle relaxants, sleeping pills, over-the-counter drugs), and to polydrug misus, but not to high misuse of stimulants. In multivariate models, after controlling for demographics, syndemic problems significantly increased the odds of high misuse of prescription opioids (OR=1.38), tranquilizers (OR=1.42), other pills (OR=1.37) and the odds of polydrug misuse (OR=1.25).
Conclusions: Our data support the conclusion that syndemic of discrimination and mental health problems has an effect on prescription drug misuse among YMSM. Practitioners should consider these findings when developing interventions that address prescription drug misuse in YMSM.
Financial Support: NIDA R36DA034543

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THE ASSOCIATION BETWEEN IL-6 AND NEUROCOGNITIVE PERFORMANCE AS A FUNCTION OF SELF-REPORTED LIFETIME MARIJUANA USE.

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Aims: The aim of the current study was to determine if self-reported lifetime marijuana use moderates the relationship between interleukin-6 (IL-6) and neurocognitive function.
Methods: We examined this hypothesis in a 161 African American adults (N = 161), including 81 women and a mean age of 45.24 (SD = 11.34). Serum was drawn upon entry into the study and the participants completed a demographic questionnaire, which included drug use history. Participants also completed a battery of neuropsychological tests.
Results: Employing regression analyses and adjusting for demographic covariates, the interaction term of IL-6 and self-reported lifetime marijuana use IL-6 was significantly associated with the both the Written (β = -.116, Standard Error [SE] = .059 p = .049) and Oral trials (β = -.143, SE = .062 p = .022) of the Symbol Digit Modalities Test as well as the Trail Making Test A (β = -.157, SE = .071 p = .028).
Conclusions: The current findings extend previous literature, which presents the inverse relationship between IL-6 and neurocognitive dysfunction. Potential protective properties of marijuana use in African Americans, who are at increased risk inflammatory or metabolic diseases, are discussed. Potential issues with marijuana abuse are also presented. Examining the potential moderating role between IL-6 and neurocognitive performance may be informative to the development of clinical interventions for inflammatory diseases.
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GLUA1 PHOSPHORYLATION: A POTENTIAL MECHANISM TO ATTENUATE COCAINE SEEKING IN RATS.

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Aims: Altered glutamatergic signaling in several brain regions, including the nucleus accumbens (NAC), has been identified as an important mediator of relapse. Specifically, the GluA1 subunit of the AMPA receptor appears to be extremely important in drug craving. Therefore, we hypothesized that drugs that attenuate cocaine seeking (the combination of metyrapone (MET) and oxazepam (OX)) will increase expression and phosphorylation of the GluA1 subunit.
Methods: Rats (n=8/group) were implanted with indwelling jugular catheters and trained to self-administer cocaine (0.25 mg/kg/infusion). Each infusion of cocaine was paired with a tone and house light cue so that the cues became secondary reinforcers. Once stable responding was achieved, rats were placed into abstinence. The day after abstinence, rats underwent a 15-minute cue-reactivity session. During this session rats were placed back in the chamber and lever presses resulted in the presentation of the secondary reinforcers; no cocaine was delivered. Rats were pretreated with either the combination of MET (50 mg/kg) and OX (10 mg/kg) or vehicle thirty minutes before the cue-reactivity session. The amygdala (AMY), NAC, prefrontal cortex (PFC), and striatum were dissected immediately after the session. Samples were analyzed for total tissue dopamine content via HPLC. Expression of total and phospho-GluA1, total and phospho-CaMKII, and total tyrosine hydroxylase (TH) was determined via Western blot. Data were analyzed using a t-test.
Results: Pretreatment with MET-OX significantly attenuated cocaine seeking, but did not result in significant differences in dopamine content or total expression of GluA1, CaMKII, or TH in any brain region. However, rats pretreated with MET-OX had significantly higher GluA1 phosphorylation at Ser831 in the AMY, NAC, and PFC. CaMKII phosphorylation was also increased in the AMY and NAC.
Conclusions: These data suggest that increased phosphorylation of the GluA1 subunit may be a neurobiological mechanism by which MET-OX attenuates cocaine seeking.
Financial Support: No outside funding.

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PRESCRIPTION DRUG USE IN A NATIONAL SAMPLE OF FEMALE DRIVERS.

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Aims: Prescription drug (Rx) use and driving is receiving increasing attention. Some Rx drugs are considered dangerous to use while driving. One of the largest consumer groups for these types of drugs are women. The aim this study is to examine Rx drug use among female drivers and characterize use, receipt of warnings regarding potential driving impairment, and perceived risks of using prescription drugs while driving.
Methods: The study is nested within the 2013 National Roadside Survey (NRS). The NRS uses stratified random sampling to select 60 sites in the continental U.S. for data collection. Drivers are randomly stopped and asked to complete a survey regarding their driving, alcohol use, and drug use. Sex differences in Rx drug use, receipt of warnings, and perceived risks were examined using Chi-square tests.
Results: To date, 6,279 drivers consented to NRS participation (from 44 sites). Of these 5,301 (84%) completed an Rx drug survey of which 2,226 (42.0%) were female. Female drivers were significantly more likely than males to report using the following drugs: antidepressants (11.8% vs. 4.4%, p<0.01), sleep aids (3.6% vs. 2.2%, p<0.01), pain killers, (3.4% vs. 2.6%, p=0.04), benzodiazepines (3.3% vs. 1.0%, p<0.01), and dietary suppressants (1.7% vs. 0.5%, p<0.01). Regarding receipt of warnings about using drugs and driving, women more often reported receiving package warning while using sleep aids (92.9% vs. 76.9%, p=0.01). There were few sex-specific differences in perceived risks of driving while taking Rx drugs; however, significantly more women than men thought it likely that ADHD medications could affect safe driving (32.5% vs. 14.9%, p=0,05) and that muscle relaxants could lead to arrest for impaired driving (64.6% vs. 44.7%, p=0.05).
Conclusions: Women were significantly more likely than men to report recent use of certain Rx drugs that could impair driving. Although the percent of women reporting warnings about use and driving was higher than for men, there remains a need to educate them as their risk perceptions related to safe driving are low.
Financial Support: National Highway Traffic Safety Administration and the National Institute on Drug Abuse

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A TYPOLOGY OF PRESCRIPTION DRUG MISUSE: A LATENT CLASS APPROACH TO CONTEXTS AND RISKS.

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Aims: Prescription (Rx) drug misuse has grown considerably in the U.S. over the past decade. Rates of Rx drug abuse are highest among young adults, for whom elevated rates of misuse occur for a range of Rx drug classes, including pain killers, sedatives and stimulants.
Methods: We use Latent Class Analysis (LCA) to identify a typology of Rx drug misusers by frequency of use among a sample of young adult Rx drug misusers. We entered the number of days subjects used Rx stimulants, pain killers, and sedatives. Because these variables were counts and there was a preponderance of zeroes, we specified a zero-inflated Poisson LCA. We evaluate differences in class membership by demographic factors and assess the relationship between class membership and health outcomes, including indications of dependence, problems associated with alcohol and drug use, and mental health.
Results: We identified a four-class solution to these patterns of Rx drug misuse: dabblers, primary stimulant users, primary downers users, and heavy users. Models indicate that the four classes did not differ significantly on any demographic variables of interest. The four groups differed significantly from each other on both the CIDI and the SIP-AD. Dabblers had the lowest scores on these measures of dependence and problems, the uppers had the next highest score, followed by the downers. Heavy users had the highest scores on both measures. No significant differences emerged when analyzing AUDIT scores. The heavy users group had significantly higher scores across three BSI subscales, suggesting a high level of mental health difficulties among this group.
Conclusions: We identified four different types of Rx drug misuse among young adults. Demographic factors did not predict group membership. Increasing frequency of use predicted dependence symptoms and self-reported problems related to Rx drug misuse. Heavy users reported significantly higher mental health problems. Targeting of frequent users of multiple Rx drug types is critical to facilitate health promotion efforts among young adults.
Financial Support: NIDA R01DA025081

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SYNTHETIC CANNABINOID USE AMONG TREATMENT SEEKING SUBSTANCE USERS.

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Aims: The purpose of this study was to characterize synthetic cannabinoid use among treatment seeking substance users. We hypothesized that marijuana smokers would be more likely to be users of synthetic cannabinoids than would individuals using other drugs. Exploratory analyses compared demographic characteristics between users and non-users.
Methods: Human subjects presenting for evaluation at the Substance Treatment and Research Service clinic at Columbia/New York State Psychiatric Institute completed a 14-item survey. Data is reported as percentages, means, and odds ratios with confidence intervals; significance was tested with Pearson's chi-squared.
Results: 75 of 287 participants (26.1%) reported using synthetic cannabinoids. Odds of using were significantly higher for participants who were not employed full-time (vs. full-time: OR = 2.81; 95%CI = 1.35, 5.81; X2 = 8.17; p = 0.004) and for those identifying as Black (Black vs. Caucasian: OR = 2.53; 95%CI = 1.30, 4.95; X2=7.63; p = 0.0057; Black vs. Hispanic: OR = 2.27; 95%CI = 1.16, 4.46; X2=5.83; p = 0.016). Marijuana (MJ) users did not have higher odds ratios for synthetic cannabinoid use compared to other drug users (MJ vs. cocaine: = 1.41; 95%CI = 0.69, 2.88; X2 =0.91, p = 0.34; MJ vs. Opiates: OR = 1.075; 95%CI = 0.53, 2.19; X2 =0.04, p = 0.84). Odds ratios were not significantly different by gender, age, or education years. Frequency of use was low, with a mean of 5.4 times/year.
Conclusions: A clinically significant proportion of treatment seeking substance users reported infrequent synthetic cannbinoid use. Less than full-time employment and Black race may be risk factors for use; marijuana smoking did not appear to increase risk. Asking about use can identify patients who may benefit from continued monitoring, however more extensive toxicology screening is not supported.
Financial Support: Supported by: National Institutes on Drug Abuse (DA009236), National Institutes on Drug Abuse (T32DA007294-19)

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DSM-5 SUBSTANCE USE DISORDER VS. DSM-IV SUBSTANCE ABUSE AND DEPENDENCE AMONG PEDIATRIC PATIENTS.

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Aims: To examine the concordance between DSM-5 and DSM-IV diagnoses for nicotine, alcohol, and cannabis in a sample of adolescent primary care patients.
Methods: 525 adolescents 12-17 years old awaiting primary care appointments in Baltimore, Maryland were recruited for a study evaluating a substance use screening instrument. Participants were assessed for DSM-5 alcohol, nicotine, and cannabis use disorder, DSM-IV alcohol and cannabis abuse, and DSM-IV dependence for all three substances during the past year using the modified Composite International Diagnostic Interview-2, Substance Abuse Module. Contingency tables examining DSM-5 vs. DSM-IV joint frequency distributions for each substance were examined.
Results: Substance use diagnoses were more prevalent using DSM-5 criteria compared with DSM-IV for nicotine (4.0% vs. 2.7%), alcohol (4.6% vs. 3.8%), and cannabis (10.7% vs. 9.0%). Cohen's κ, Somer's *d*, and Cramer's V ranged from .47 to .82 for all three substances. Of the adolescents categorized as sub-threshold under DSM-IV, 7 of 16 (43.8%), 9 of 29 (31.0%), and 10 of 33 (30.3%) met criteria for DSM-5 disorder for nicotine, alcohol, and cannabis, respectively. Additionally, 5 of 17 (29.4%) and 1 of 19 (5.3%) adolescents who met criteria for DSM-IV abuse did not meet criteria for a DSM-5 diagnosis for alcohol and cannabis, respectively.
Conclusions: Categorizing adolescents using DSM-5 criteria may result in net widening—particularly for cannabis—by capturing adolescents in the DSM-5 substance use disorder classification who were sub-threshold using DSM-IV criteria. More research is needed to examine the validity of DSM-5 nicotine, alcohol, and cannabis use disorders with larger and more diverse adolescent samples.
Financial Support: NIDA: R01 DA026003-03S1

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D-AMPHETAMINE EFFECTS AND MONETARY INCENTIVE DELAY TASK PERFORMANCE: AN FMRI STUDY.

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Aims: Impulsivity, a biologically based trait composed of independent behavioral processes of reinforcement-based activation and punishment-based inhibition, has been linked to drug abuse vulnerability. This study examined d-amphetamine effects on brain responses during monetary incentive delay (MID) task performance as a function of sensation-seeking and inhibition dimensions of impulsivity.
Methods: Forty young healthy adults scoring in the upper and lower median of population norms on inhibition and sensation seeking items of the Zuckerman-Kuhlman Personality Questionnaire completed a 4-session study examining the effects of d-amphetamine (0, 15 mg/70 kg, IN) on MID task performance during fMRI assessment. MID task consisted of reinforcement (i.e., earn $0.05 or $0.50), avoidance (i.e., avoid losing $0.00 or $0.50) and control ($0) reaction-time trials consisting of cue, target and feedback phases. Task performance, brain activation, verbal reports and cardiovascular data are analyzed using ANOVA.
Results: MID task performance engenders brain activation in thalamo-striatal regions in the cue phase and in the caudate nucleus during the feedback phase. Intranasal d-amphetamine engendered significant stimulant effects, including increased heart rate (6.3 bpm) and systolic (8.0 mmHg) and diastolic (5.8 mmHg) blood pressure.
Conclusions: The effects of d-amphetamine on brain activation associated with monetary incentive and trial contingencies (i.e., reinforcement, avoidance) will be examined as a function of sensation-seeking and inhibition to determine the role of reinforcement processes associated with impulsivity and drug abuse vulnerability.
Financial Support: Supported by DA-05312.

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INTOXICATION AT LAST SEXUAL INTERCOURSE AND UNPROTECTED SEX AMONG HIV-POSITIVE AND HIV-NEGATIVE INDIVIDUALS IN UGANDA: AN EVENT-LEVEL ANALYSIS.

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Aims: Little is known about the intoxication-unprotected sex association among HIV-positive and negative individuals in Sub-Saharan Africa. This study examined the association between intoxication at last sexual intercourse and unprotected sex among HIV-positive and negative individuals in Uganda.
Methods: The data used in this study was the 2011 nationally representative Uganda AIDS Indicator Survey. Face-to-face interviews were conducted with 9,588 men and 12,153 women aged 15-to-59 years yielding a response rate of 97%. Blood samples were collected to test for HIV sero-status with response rates exceeding 95%. Logistic regression analyses were conducted among HIV-positive and HIV-negative individuals, adjusted for sociodemographic and behavioral covariates that were also examined as moderators.
Results: The intoxication-unprotected sex association was found among HIV-negative individuals (adjusted odds ratio (AOR) = 2.67; 95% confidence interval (CI) = 1.30 – 5.48) who knew that condoms prevent HIV, an association not found among HIV-negative respondents who were aware that condoms prevent HIV (AOR = 1.21; 95% CI = 1.00 – 1.46). Intoxication was also associated with unprotected sex among HIV-positive individuals (AOR = 1.45; 95% CI = 1.30 – 5.48) and no covariate moderated the relationship.
Conclusions: The results suggest that the intoxication-unprotected sex link be incorporated within Ugandan national strategies among HIV-positive and negative individuals. HIV-negative individuals who are unaware that condoms prevent HIV should be targeted for interventions focusing on increasing HIV transmission knowledge, especially the role of condoms in preventing the disease. The latter interventions should also identify those sociocultural and political beliefs about condom use that may serve as barriers to consistent condom use and differences in sociocultural norms that govern HIV-positive and negative individual's motivation to use condoms.
Financial Support: NIDA (F32DA0364431: Dr. Kerridge); Columbia University, Mailman School of Public Health (Dr. Hasin).

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SLEEP QUALITY IN PATIENTS WITH SUD AND BEHAVIORAL ADDICTIONS ASSESSED BY ACTIGRAPHY : A PROSPECTIVE STUDY.

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Aims: Previous studies showed an association between sleep and addiction. Sleep disorders during treatment may increase the risk of relapse in subtance use disorder patients. However, most of these studies reported subjective measures and were generally limited to a single substance use disorder. The aim of our study was to describe the quality of sleep in subjects with substance use disorders or/and behavioral addictions by using an objective and noninvasive measure, the actigraphy, at treatment entry and 12 months thereafter.
Methods: Subjects were recruited at their entry in treatment in an outpatient addiction clinic. Subjects wear the actigraphy device for 7 days and 7 nights in a row, without changing anything in their daily activities. The actigraphy measures were performed at baseline and after 1 year of treatment. Actigraphy provided several measures: total sleep time (TST), duration of nocturnal awakenings (NA), sleep latency (SL) and sleep efficiency (SE).
Results: 62 subjects (59% males, 39 y.o) had a mean SE of 82.5% (SD=6.8), a mean SL of 16.9 min (SD= 13.6), an average total time of NA of 59.6 min (SD=27.5) and TST of 6h 48min (SD= 60min 12sec). About two-third of the subjects (67%, n=42) exhibited an impaired quality of sleep (i.e.<85%) at baseline. 12-month follow-up analysis revealed an improvement in quality of sleep.
Conclusions: Subjects exhibited an impaired quality of sleep compared to general population (higher duration of NA and lower SE and TST) but it seems that these variables improved after 12 months of treatment analysis.
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SUBSTANCE USE AND STI/HIV RISK AMONG AFRICAN-AMERICAN MEN INCARCERATED IN NORTH CAROLINA.

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Aims: To describe associations between pre-incarceration substance use and sexually transmitted infection (STI) and HIV risk among incarcerated African American men. Substance use will be associated with STI/HIV risk. Crack use will be a strong correlate.
Methods: Project DISRUPT is an ongoing cohort study among African American men being released from prison who were in committed partnerships with women at prison entry. Data collected prior to release (N=180) were analyzed to assess substance use six months before incarceration and sexual risk-taking six months before incarceration and infection with chlamydia, gonorrhea, or trichomoniasis measured prior to release using urine-based nucleic acid amplification assays.
Results: Respondents reported marijuana use (daily: 46%, weekly: 56%), binge drinking (daily: 10%, weekly: 48%), and ecstasy (12%), powder cocaine (12%), and crack (11%) use. Non-injected heroin, methamphetamine, hallucinogens, and injection drugs were reported by 1% or less. Multiple (47%) and concurrent (36%) partnerships and sex trade (9%) were common, and 7% had an STI. When adjusting for age, poverty, and depression, daily binge drinking was associated with multiple partnerships (OR: 6.73, 95% CI: 1.73-26.10), concurrency (OR: 5.95 95% CI: 1.82-19.40), sex trade (OR: 4.10, 95% CI: 1.08-15.60), and any STI (OR: 4.29, 95% CI: 1.13-16.40). Marijuana use was associated with multiple partnerships; ecstasy use with multiple/concurrent partnerships; and powder cocaine, but not crack, use with sex trade.
Conclusions: Among African American incarcerated men, different substances were linked to different patterns of HIV/STI risk. Crack use surprisingly was not a correlate.
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RISK FACTORS FOR CONSUMPTION OF ENERGY DRINKS, ALCOHOL AND BOTH AMONG A SAMPLE OF YOUTH FROM 10 U.S. METROPOLITAN AREAS.

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Aims: Energy drink and alcohol consumption have become increasingly popular among youth. We had the opportunity to investigate risk factors for these behaviors among youth living in 10 metropolitan areas who consumed in the 7 days prior to their interview: (1) neither alcohol nor energy drinks; (2) alcohol alone; (3) energy drinks alone; or (4) both. We also compared the sociodemographic and risk factors associated with these consumption patterns.
Methods: The National Monitoring of Adolescent Prescription Stimulants Study (N-MAPSS) assessed behaviors and risk factors from 11,048 youth, 10 to 18 years of age, at entertainment venues in urban, suburban and rural areas of 10 US metropolitan regions. In addition to questions on lifetime nonmedical use of prescription stimulants and past 30 days tobacco and marijuana use, youth were asked questions to assess sociodemographic and risk factors such as grades in school, perceived health status and household composition. Energy drink and alcohol consumption were also assessed.
Results: Among the sample of 11,040 youth with complete data, 57.3% reported neither alcohol nor energy drink consumption, 7.2% reported alcohol, but not energy drink consumption, 26.7% reported energy drink, but not alcohol consumption, and 8.8% reported consuming both. Multivariate logistic regression indicated increased odds of drinking both energy drinks and alcohol among those with tobacco, marijuana and nonmedical use of prescription stimulants.
Conclusions: This first study of energy drink consumption among a sample that included 10 and 11 year olds from across the US showed that energy drink consumption is common, that energy drink consumption alone is not predicted by use of tobacco or marijuana, but use of both alcohol and energy drinks is predicted by such use. Capturing quantity and patterns of both energy drink and alcohol consumption will contribute to greater understanding of the nature of such use among youth.
Financial Support: NMAPSS was conducted under contract with Pinney Associates, Inc., with funding provided by Shire Development LLC and Noven Pharmaceuticals.

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PRESCRIPTION OPIOID USE IS ASSOCIATED WITH INCREASED MORTALITY IN THE REASONS FOR GEOGRAPHIC AND RACIAL DIFFERENCES IN STROKE STUDY.

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Aims: Prescription opioid use (POU) for chronic non-malignant pain has increased in the US over the last decade. Previous research has demonstrated increased mortality related to POU overdose or abuse but population-based studies have not examined the relationship between POU and all cause mortality (ACM), adjusting for a variety of underlying chronic conditions as well as levels of chronic pain, which was the purpose of this study
Methods: POU was examined in 30,239 participants of the REGARDS study, a national cohort of community-dwelling black and white adults aged ≥ 45 years recruited between 2003 and 2007. Persons receiving cancer treatment were not eligible. Baseline data were collected through a telephone survey and an in-home study visit. POU was ascertained at baseline via pill bottle review. Telephone follow-up was conducted every 6 months, and deaths were expert-adjudicated based on review of medical records, interviews with family members, death certificates and autopsy reports. Sequentially adjusted Cox proportional hazards models examined associations of POU with ACM, overall and stratified by gender, controlling for socio-demographics, behaviors, physiological measures, self-reported health status, chronic diseases and chronic pain at baseline.
Results: Compared to the 27,174 non-users, the 2427 (8.2%) participants using POUs did not differ in mean age (64.9±9.4 vs. 64.7±9.4, p=0.34) but included fewer men (33.6% vs. 45.9%, p <.001) and more blacks (45.2% vs. 40.7%, p < .001). Over a median follow up of 5.3 years, there were 400 and 2,742 deaths in those using and not using POUs. In the fully adjusted analysis, POU was associated with an increased risk for ACM (hazard ratio [HR]=1.24, 95%CI: 1.08-1.42). ACM was increased among women (HR=1.35, 95%CI: 1.12-1.64) but not men (HR=1.09 95%CI: 0.89-1.33; p for interaction 0.09).
Conclusions: POU in this community sample was independently associated with increased mortality, especially among women.
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COCAINE ADDICTION: ROLE FOR GLUTAMATE, GLIA AND CHEMOKINE.

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Aims: The aim of the study is to investigate the effect of novel activators of glutamate transporter (GLT-1), ceftriaxone (CTX) and clavulanic acid (CLAV), on drug taking and seeking behavior. In addition, glial cell activity after cocaine exposure and during short and long-term withdrawal has been examined. Furthermore, possible involvement of chemokine receptor, CXCR4, in cocaine reward was examined.
Methods: The effect of CTX and CLAV was tested in mouse intravenous self-administration model. Acquisition of self-administration under fixed-ratio (FR) schedule of reinforcement was used as a measure of drug-taking behavior, and progressive ratio (PR) schedule of reinforcement was used to assess drug-seeking behavior. In a separate study, rats were injected with cocaine (15mg/kg, i.p.) for 7 consecutive days, and glial cell activity was investigated using immunofluorescence microscopy at 2hr, 2, 10 and 30 days after last injection. Effect of AMD3100, a CXCR4 antagonist, on development of cocaine conditioned place preference was tested.
Results: CTX and CLAV pretreatment decreased cocaine intake in mice maintained under the PR of reinforcement. However only the CTX not CLAV pretreatment was able to decrease acquisition of self-administration in mice under FR schedule of reinforcement. There was a significant increase of astrocytic activation in nucleus accumbens of rats withdrawn from cocaine for 30 days. AMD3100 attenuated development of cocaine conditioned place preference.
Conclusions: GLT-1 activators are able to decrease reinforcing strength of cocaine by increasing the extracellular glutamate reuptake. Astrocyte activity is increased in nucleus accumbens of rats in long-term cocaine withdrawal. Attenuation of cocaine conditioned place preference by AMD3100 suggests a role for chemokine receptor in drug reward.
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R21 DA043718

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MDPV-INDUCED CONDITIONED TASTE AVERSIONS IN THE F344/N AND LEW RAT STRAINS.

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Aims: The inbred Fischer (F344) and Lewis (LEW) rat strains have been used to study genetic differences in a wide variety of physiological and behavioral endpoints, including responsiveness to cocaine. Specifically, LEW rats show greater sensitivity to the aversive effects of cocaine than F344 rats. Like cocaine, MDPV ("Bath Salts") is a dopamine (DA) reuptake inhibitor, although it is more efficient and potent than cocaine in this respect. MDPV also possesses aversive properties, making it a good candidate to assess whether the aforementioned strain differences with might be mediated through its effects on DA.
Methods: Male F344 and LEW rats were exposed to a conditioned taste aversion procedure in which exposure to a novel saccharin solution was followed by injections of one of four doses of MDPV (0, 1, 1.8 and 3.2 mg/kg). Animals had four saccharin-MDPV pairings, followed by a final two-bottle test. Aversions were assessed by comparing saccharin consumption across trials, as well as percent saccharin consumption on the two-bottle test. Data were analyzed with ANOVAs, followed by tests of simple effects as appropriate.
Results: MDPV induced robust dose-dependent taste aversions with near total suppression at the highest dose of MDPV administered. These effects were evident in both F344 and LEW rats, but there was no difference between the two strains in the rate of acquisition or the degree of the aversion.
Conclusions: The fact that there were no strain differences in MDPV-induced aversions suggests that the reported strain differences with cocaine are unlikely a function of differential DA sensitivity. Given the nonspecific effects of cocaine on DA, 5-HT and NE reuptake, it is possible that other brain amines may be involved in cocaine's aversive effects in the two strains.
Financial Support: This research was supported by a grant from the Mellon Foundation to ALR and a Dean's Graduate Research Grant to HEK.

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RELATIONSHIP OF ALCOHOL AND COCAINE ON MOOD EPISODES AMONG HIV-INFECTED ADULTS WITH BIPOLAR DISORDER AND MAJOR DEPRESSIVE DISORDER.

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Aims: Mood disorders, such as bipolar disorder (BD) and major depressive disorder (MDD), are disproportionately prevalent among HIV-infected individuals, and comorbid substance abuse is also common. Depression has been found to be associated with faster HIV disease progression, and mania with HIV transmission risk behaviors. Fluctuations in substance use over time may affect mood symptomatology, but this has not been empirically examined. This study examined the weekly associations between mood episodes and substance use over a 12-week period.
Methods: Participants were 59 HIV-infected adults with mood disorders (n = 23 with BD and n = 36 with MDD) recruited from Infectious Disease clinics. Psychiatric disorders were identified using the Mini International Neuropsychiatric Interview. Weekly frequency of substance use was assessed using the Timeline Follow-back, and weekly mood symptoms were assessed using the Longitudinal Interval Follow-Up Evaluation. Mixed model analyses were used to examine the association between weekly substance use and mood episodes.
Results: 83% of BD patients and 64% of MDD patients had mood episode(s) in the past 12 weeks. 37% reported heavy alcohol use, and 53% reported cocaine/crack-cocaine use. In mixed model analyses, heavy alcohol use was strongly associated with the occurrence of a depressive episode ($p<.001$) and cocaine use with mania ($p = .003$).
Conclusions: These results suggest that substance use and mood episodes are associated, perhaps with bi-directional effects. Given the high incidence of mood episodes in this sample, there are clearly unmet mental health needs in HIV-infected individuals. It is crucial that health care providers integrate substance abuse and psychiatric treatment in Infectious Disease clinics. Identifying specific links between substance use and mood could lead to better prediction, prevention and treatment of HIV/AIDS-risky behaviors.
Financial Support: P10 AI-064518

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ILLICIT DRUG USE HARMS RESPONSE TO PSYCHIATRIC TREATMENT.

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Aims: Studies evaluating the efficacy of psychiatric treatment for opioid-dependent individuals have yielded inconsistent findings. This study evaluates if illicit drug use at the start of psychiatric care affects treatment response.
Methods: Methadone maintenance patients with at least one co-occurring psychiatric disorder completed a 3-month randomized clinical trial evaluating the efficacy of on-site integrated substance abuse and psychiatric care (Kidorf et al., 2013). The present study re-analyzes the data set by grouping participants into one of two conditions: 1) no baseline opiate, cocaine or sedative use (n = 50), or 2) baseline opiate, cocaine or sedative use (n = 75). All participants received a similar schedule of psychiatric care, and had good access to prescribed psychiatric medications. The Global Severity Index (GSI) of the Hopkins Symptom Checklist-Revised was administered monthly to evaluate changes in psychiatric distress.
Results: Results showed that while both conditions evidenced similar utilization of on-site psychiatric services, participants with no baseline drug use remained in treatment somewhat longer (80.7 vs. 74.8 days, $p = .05$) and demonstrated greater reductions in GSI scores (-6.96
vs. -2.91, $p = .02$) than participants with baseline drug use.
Conclusions: These results have implications for interpreting previous studies that have shown inconsistent efficacy of psychiatric pharmacotherapy, other psychiatric treatment, and provision of clinical care for patients with co-occurring substance use and psychiatric disorders.
Financial Support: DA028154-02 from NIDA

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STUDY ATTRITION AMONG HIV-INFECTED RUSSIAN RISKY DRINKERS.

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Aims: Participant attrition in HIV longitudinal studies may diminish research quality. Awareness of participant characteristics predictive of attrition is limited in Eastern Europe. The study aimed to identify factors associated with attrition among HIV-infected risky drinkers from an HIV prevention trial in Russia. We examined whether current injection drug use (IDU), binge drinking, depression, HIV non-disclosure, stigma and lifetime history of incarceration were predictors of attrition. We also explored effect modification due to gender.
Methods: The trial had assessments at baseline, 6 and 12 months. Loss to follow-up (LTFU), defined as no follow-up visits after baseline, was the primary outcome, and the secondary outcome, time to first missed visit, was defined as the time from baseline to first missed visit (i.e. 6 or 12 months), with censoring at end of study or death. We used multiple logistic regression models for the primary analysis, and Cox proportional hazards models for the secondary analysis.
Results: Of 660 participants, 101 (15.3%) had no follow-up. No significant associations between independent variables and LTFU were observed. In secondary analysis, current IDU (AHR 1.39, 95% CI 1.03, 1.87) and HIV non-disclosure (AHR 1.38, 95% CI 1.03, 1.86) were significantly associated with missing a follow-up visit. Gender stratified analyses suggested a larger impact of binge drinking among males and incarceration history among females for missing a follow-up visit.
Conclusions: Current IDU and HIV non-disclosure were significantly associated with a missed follow-up visit among HIV-infected Russian risky drinkers. Understanding predictors of attrition may inform efforts to improve participant retention in research studies.
Financial Support: The study was supported by NIH grants R01AA016059, U24AA020778, U24AA020779 and K24AA015674. Dr. Kiriazova was supported by a NIDA INVEST Fellowship.

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PRELIMINARY EVIDENCE OF INJECTING DRUG REDUCTION FROM A WOMAN-FOCUSED RCT IN REPUBLIC OF GEORGIA.

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Aims: Women with substance use disorders are one of the most hidden and underserved populations in Georgia (GEO). Women comprise only 2% of the patient population in substance use treatment in GEO, and research examining patterns of substance use in GEO women is lacking. The purpose of the study was to develop an intervention that would reduce illicit substance use and the rate of HIV infection.
Methods: In this RCT intervention group participants received a structured 12-session intervention focusing on HIV/HCV prevention, mental and physical health, drug and alcohol use prevention during pregnancy, while usual care group participants received information and case management for 12 sessions. Urine drug screening was conducted at each session and assessments were conducted at baseline and 1&3-month follow-up. Eligibility criteria included injection of illicit drugs in the past 30 days verified by venous stigmata and sexually active at least once in the past 30 days.
Results: Preliminary data on 64 cases showed opioids (mainly desomorphine: "crocodile") were the most commonly injected drugs (64%) during the past 30 days, followed by homemade stimulants (33%). Concomitant use of benzodiazepines (56%) and barbiturates (10%) was common. Results of urine screening revealed that stimulant and benzodiazepine use declined over time irrespective of condition (ps<.02).
Conclusions: Reaching this stigmatized and hidden population is essential to the welfare of families. Preliminary findings suggest either intervention? resulted in a marked reduction in use of illicit substances in both groups. Interventions that are women-centered, accessible, confidential, receptive, and provide a non-judgmental and caring environment are beneficial for women with substance-use-related problems.
Financial Support: Supported by NIDA R01DA029880

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OPIOID SYSTEM LOCATED DOWNSTREAM OF α7 NICOTINIC ACETYLCHOLINE RECEPTOR PARTICIPATES IN THE DEVELOPMENT OF PHYSICAL DEPENDENCE ON NICOTINE IN MICE.

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Aims: We previously reported that nicotine (NIC)-induced analgesia, but not glucocorticoid increase, was suppressed by opioid receptor antagonist, naloxone (NLX), indicating that nicotine effect is mediated in part by the activation of the endogenous opioid system. Moreover, it is well known that NIC has physical-dependence liability, but its mechanism is still unclear. Therefore, we examined whether physical dependence on NIC was mediated by activation of the opioid system. Furthermore, we clarified nicotinic acetylcholine receptor (nAChR) subtype connected to the opioid system.
Methods: The activation of hypothalamic-pituitary-adrenal axis, i.e. serum corticosterone (SCS) increase, was employed as an indicator of NIC withdrawal sign. Firstly, we studied the effects of doses and periods of repeated NIC treatments on NLX-precipitated SCS increase using ICR mice. Secondary, we investigated the effects of concomitant treatments of opioid receptor antagonist or nAChR subtype antagonist with repeated NIC on NLX-precipitated SCS increase. Naltrexone (NTX) was employed as opioid receptor antagonist. And methyllycaconitine (MLA) and dihydro-β-erythroidine (DHβE) were used as α7 nAChR antagonist and α4β2 nAChR antagonist, respectively. SCS levels were quantified by fluorometric assay.
Results: In this study, NLX precipitated an SCS increase in mice receiving repeated NIC, by a dose-dependent mechanism, and correlated with the dose and number of days of repeated NIC administration. When NTX was concomitantly administered with repeated NIC, the NLX-precipitated SCS increase was not elicited. Concomitant administration of MLA with repeated NIC, but not DHβE, did not elicit an SCS increase by NLX.
Conclusions: A physical dependence on NIC was in part developed by the activation of the endogenous opioid system, and the opioid system was located on the downstream of α7 nAChR. This opioid component in physical dependence on NIC might be a useful target for the cessation of tobacco smoking.
Financial Support: This work was supported by a grant from the Smoking Research Foundation.

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DOES THE EFFICACY OF MEDICATIONS FOR SUBSTANCE ABUSE TREATMENT DECREASE OVER TIME?

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Aims: Prior research suggests the efficacy of some medications decline over time. A previous study suggests this trend may occur with nicotine replacement therapies (NRT) because remaining users are more difficult to treat. The present research aims to test this hypothesis by exploring 1) more recent trials of medications to treat tobacco use disorder, 2) medications to treat alcohol and opioid use disorder.
Methods: Data were acquired from randomized controlled trials in the Cochrane Database. The analyses included abstinence rates from 122 NRT trials from 1979 to 2012 (N=51,265), 24 acamprosate trials from 1985 to 2006 (N=6,172), and 26 naltrexone trials from 1992 to 2008 (N=4,693). We examined the incidence of a) abstinence in the active condition, b) abstinence in the control condition, and c) the active vs placebo effect size via the Odds Ratio (OR). Thus, we conducted 9 fixed-effects meta-analyses (3 drugs x 3 outcomes). We then conducted regressions evaluating the effect of time in which study weights were determined by their sample size. Further analyses from methadone and buprenorphine trials will be included in the presentation.
Results: The rate of abstinence from alcohol decreased over time in participants treated with acamprosate (-15%/10yrs; p<.01) but did not change in the controls; the OR decreased over time (-1.00/10yrs; p<.05). The rate of abstinence from heavy drinking in participants treated with naltrexone appeared to decrease (-27%/10yrs; p<.10), but did not change in controls. The naltrexone treatment OR appeared to decrease (-.72/10yrs; p<.10). In NRT studies, the rate of abstinence in controls decreased (-1.20%/10yrs; p<.05) but the active group and the OR did not change over time.
Conclusions: Our hypotheses that the OR would decrease over time was partially supported. Analyses exploring time effects with methadone and buprenorphine, and possible explanations for the differences in medication efficacy will be discussed.
Financial Support: This work was supported by NIDA 5 T32 DA 7242-23.

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EFFECTS OF DISSEMINATION EFFORTS TO PROMOTE CLIENT ENGAGEMENT IN RECOVERY-ORIENTED ACTIVITIES IN COMMUNITY-BASED TREATMENT.

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Aims: Involvement in positive activities (e.g. physical, recreational, spiritual, and sober socializing) contributes to improved quality of life, a predictor of sobriety and of the broader goal of recovery. Using data from NIH-funded studies, we examined whether having a counselor trained to target positive activities in treatment planning increases clients' involvement in such activities at 3-month follow-up.
Methods: One group of clients was recruited prior to counselor training, with a second group at post-training. Counselor training consisted of a day-long session on evidence-based practices for individualized treatment planning. A 1-hour module emphasized the importance of clients' involvement in positive activities.
Results: Treatment plan and 3-month follow-up data were available for 217 clients (Pre-training N=132; Post-training N=85). At follow-up, rates of at least one day in the past 30 days involvement in positive activities were high (>90%) in both groups. However, in multilevel analyses (nesting clients within sites) post training clients were significantly more likely (OR=5.8, p<0.001) to have involvement in positive activities noted on their treatment plan and to report being involved in positive activities for at least 30 of the past 90 days (OR=4.3, p<0.001).
Conclusions: Training counselors to encourage clients' involvement in positive activities as part of the treatment planning process may be an effective strategy to promote behaviors previously identified as predictors of sobriety and recovery outcomes. Future studies are needed to identify which positive activities are related to abstinence and how to best encourage the workforce to foster these activities in the recovery process.
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AVAILABILITY OF SMOKING CESSATION SERVICES IN SUD TREATMENT IN THE CONTEXT OF HEALTH REFORM.

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Aims: Smoking is highly prevalent among persons with substance use disorders (SUDs). Many patients would benefit from greater integration of smoking cessation services in SUD treatment, yet little is known regarding the associations between treatment funding sources and the availability of such services. Given that health reform will likely increase Medicaid and private insurance coverage for persons with SUDs, this study examines the hypothesis that these funding sources are associated with the availability of smoking cessation services in a national sample of SUD treatment organizations.
Methods: Face-to-face interviews were conducted in 2009-2012 with directors of 308 treatment organizations. Key measures were: (1) an index of 6 brief interventions, (2) presence of a formal smoking cessation program; and (3) adoption of any FDA-approved medication (i.e., nicotine replacement, varenicline, bupropion). Funding measures were percentages of past-year revenues from Medicaid, private insurance, and other governmental sources. Organizational structure, size, and workforce professionalism were controlled.
Results: The average SUD program had adopted 3.7 (SD=1.9) of the 6 brief interventions. About 22.6% offered a formal smoking cessation program, and 26.8% had adopted at least one smoking cessation medication. Controlling for organizational characteristics, Medicaid revenues were positively associated with the index of brief interventions (beta=.15, p=.01), but not the other two services. Greater reliance on private insurance was positively associated with the index of brief interventions (beta=.19, p=.005) and medication availability (odds ratio=1.02, p=.04).
Conclusions: Availability of smoking cessation services remains limited in SUD treatment. These study findings suggest that the expansion of private insurance and Medicaid under health reform may promote the adoption of smoking cessation services, particularly brief interventions and pharmacotherapy, in specialty SUD treatment programs.
Financial Support: Supported by the National Institute on Alcohol Abuse and Alcoholism (R01AA015974).

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COCAINE-DEPENDENT ADULTS ARE MORE LIKELY THAN CONTROLS TO CHOOSE IMMEDIATE UNSAFE SEX OVER DELAYED SAFE SEX.

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Aims: Cocaine abuse and dependence have been associated with an increased prevalence of risky sexual behaviors that confer a greater chance of contracting or spreading HIV. The decision to use a condom during sex may be affected by a number of factors including the availability of a condom, attractiveness of the partner, and perceived likelihood of the partner having a sexually transmitted infection (STI).
Methods: 34 cocaine-dependent and 30 control participants completed the Sexual Discounting Task, which measures how likely a person is to use a condom during sex as a function of the delay to condom availability. From a series of photos of unknown individuals that the participant endorsed as individuals he or she would be likely to have sex with, participants choose the individual he or she found most attractive, least attractive, most likely to have an STI, and least likely to have an STI. The task was completed four times, one in regard to the picture endorsed in each of these four categories. Each task run consisted of a series of choices between having sex immediately without a condom and waiting a period of time (1 hr to 3 mo) to have sex with a condom. We hypothesized that cocaine-dependent individuals would be less likely to wait for a condom when one is not immediately available. Discount rates for safe sex were compared between groups with nonlinear regression.
Results: Despite reporting a similar likelihood of using a condom when it was immediately available, cocaine-dependent participants had a higher discount rate for safe sex in each of the four conditions, indicating a relative willingness to engage in unsafe sex if a condom is delayed in availability even a short period of time.
Conclusions: The immediacy of condom availability is important to the decision to engage in safe sex, with cocaine-dependent adults more willing to choose immediate, unsafe sex over delayed, safe sex.
Financial Support: NIDA grants R01DA030241, R01DA032363, R21DA032717, and R01DA035277

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SEX DIFFERENCES IN IMPULSIVITY AND BRAIN VOLUMES IN METHAMPHETAMINE USERS.

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Aims: Methamphetamine (METH) is an addictive stimulant known to adversely affect behavior and the brain. The aim of this study was to investigate impulsivity and brain structures, and possible sex differences on these variables, between METH users and non-drug user controls (CON).
Methods: 101 subjects completed the Barratt Impulsiveness Scale (BIS) questionnaire and structural brain MRI: 52 METH (ages 41.6±1.5 years, 30 males, 22 females) and 49 CON (ages 45.0±2.3 years, 30 males, 19 females). Automated morphometry in FreeSurfer 5.1 was used to measure brain volumes. 2-way-ANCOVA, co-varying for education, depressive symptoms, and intracranial volume, evaluated for independent and interactive effects of group status and sex. Abnormal brain volumes were correlated with BIS.
Results: METH users had higher impulsivity scores in all six factors ($p<0.0001$-0.006). All women had lower scores in attention compared to men ($p=0.02$). A group-by-sex interaction was found in perseverance ($p=0.03$); male METH users had higher scores compared to CON and female METH ($p<0.0001$-0.04). METH had larger right (R) globus pallidus ($p=0.03$) and R insula ($p=0.01$), but smaller left (L) insula ($p=0.04$). Only male METH had smaller L precentral gyrus than male CON ($p=0.06$), but only female METH had larger R accumbens than female CON ($p=0.02$). L precentral volumes negatively correlated with attention scores in females ($r=-0.36$, $p=0.02$), but not in the males (interaction-$p=0.05$).
Conclusions: Consistent with prior reports, METH users had greater impulsivity, especially in the males. METH users also had larger R globus pallidus, but smaller L insula, and male METH users tended to have smaller precentral gyrus. In women, those with larger precentral gyrus had better attention, similar to that in ADHD patients. While larger accumbens was also reported in METH users, we found this only in female METH users. The larger volume in female METH users may be due to greater neuroinflammation than in men, which may reflect a compensatory neuroprotective effect in female METH users.
Financial Support: R24DA-27318; K24DA-16170; U54NS56883; G12-MD007601

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CHILDHOOD MALTREATMENT AND AMYGDALA CONNECTIVITY IN METHAMPHETAMINE DEPENDENCE.

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Aims: Childhood maltreatment, a risk factor for the development of addiction, has been linked to brain abnormalities in adulthood. As the relationship between trauma and brain function in addiction has been relatively understudied, the goal of this work was to extend work in this area.
Methods: The relationship between scores on the Childhood Trauma Questionnaire (CTQ) and resting-state functional connectivity (RSFC) of the amygdala was assessed in 15 MA-dependent and 16 healthy individuals. In addition, self-report measures of depression, trait anxiety, and emotion dysregulation were correlated with amygdala RSFC of regions that showed a positive relationship with CTQ.
Results: MA subjects showed a positive relationship with CTQ and amygdala RSFC with hippocampus, parahippocampal gyrus, and orbitofrontal cortex ($p < 0.05$, whole-brain corrected). Amygdala RSFC with right hippocampus also was positively related to depressive affect and emotion dysregulation and negatively related to self-compassion and mindful disposition ($p's < 0.05$). The relationship between amygdala RSFC and CTQ showed no group interaction and no relationship within the control group ($p's > .05$).
Conclusions: These findings suggest that childhood trauma produces enduring differences in brain function that contribute to negative affective states and emotional dysregulation. The results raise the possibility that a history of trauma may account for the prominent hypermetabolic condition in the amygdala in MA individuals, and may contribute to a variety of addiction-related behavioral states, such as craving, which is linked with amygdala and hippocampal activation.
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REASONS FOR E-CIGARETTE INITIATION AND DISCONTINUATION AMONG ADOLESCENTS AND YOUNG ADULTS.

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Aims: E-cigarettes (e-cigs) are increasing in popularity among youth. Understanding reasons that promote and prevent initiation and encourage discontinuation is crucial to the development of effective prevention messages for youth.
Methods: We conducted 18 focus groups (6-8 participants each) in 2 colleges, 2 high schools and 2 middle schools in CT. All groups were stratified by gender and college and high school groups were also split by cigarette smoking status. A focus group manual guided discussions about reasons for use and non-use. Focus group transcripts were examined by independent raters using thematic analysis.
Results: All groups reported curiosity as a reason for experimenting with e-cigs. Influences from friends and family were a common factor related to initiation among college and high school students as were perceived easy access, desire to quit smoking, and availability of flavors. Middle school students cited novelty and perceptions that e-cig use represents a sign of independence. For high school and college smokers, reasons for discontinuation included e-cigs being less satisfying than cigarettes. College non-smokers cited loss of interest once the novelty wore off. College and high school smokers who had never tried e-cigs were deterred by the high cost. College and high school students were also hesitant to try e-cigs due to unknown health and safety risks. Both high school and middle school students described parental disapproval as a deterrent, high school students also cited friend disapproval as deterring use. Across all groups, those who had not tried e-cigs described lack of "coolness" as an additional deterrent.
Conclusions: This qualitative study indicated several reasons why youth initiated, abstained from and discontinued e-cigarettes. While there were some common themes across groups, different themes also emerged across the age groups. Understanding these factors may inform e-cig prevention messages.
Financial Support: This work was supported by the National Institute on Drug Abuse grant P50DA009241

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SAFETY AND PHARMACOKINETICS OF OXYCODONE DETERX ADMINISTERED INTRANASALLY IN RECREATIONAL OPIOID USERS.

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Aims: Oxycodone DETERx is a multi-particulate, abuse-deterrent formulation designed to retain ER properties following common methods of tampering. The purpose of this study was to assess the safety and the pharmacokinetics (PK) of crushed DETERx capsule contents administered IN (DETERx IN) compared with 2 control treatments: immediate-release (IR) oxycodone powder administered IN (Oxy IN) and intact DETERx capsules administered orally (DETERx PO).
Methods: Open-label, randomized, naltrexone-blocked, 3-treatment, 3-period, crossover comparison study. Safety and PK of 40 mg doses of DETERx IN, Oxy IN, and DETERx PO were compared in nondependent, recreational opioid users experienced with IN administration (n=13). DETERx capsule contents were crushed using the most aggressive crushing method identified in previously conducted studies. Plasma samples were collected at pre-specified time points and analyzed using a LC-MS/MS method. PK parameters Cmax, AUCINF, Tmax and Abuse Quotient (AQ) were calculated. Safety assessments included treatment-emergent adverse events, vital signs, oxygen saturation and nasal cavity assessments.
Results: Cmax LSMean ratio for DETERx IN relative to Oxy IN was 59.0%. Cmax LSMean ratio for DETERx IN relative to DETERx PO was 79.6%. DETERx IN and DETERx PO both had a median Tmax of 5.0 hrs, longer than Oxy IN (3.0 hrs). Oxy IN had the highest AQ value (42.5 ng/ml/hr); AQ values for DETERx IN and DETERx PO were similar (8.5 and 8.4 ng/ml/hr, respectively). AUCINF values were similar for all treatments. There were more spontaneously reported nasal-related AEs and a greater number of episodes of need to blow nose post insufflation of crushed DETERx compared with Oxy.
Conclusions: Crushing and snorting DETERx capsule contents produces relatively lower plasma concentrations of oxycodone compared with intact DETERx PO and Oxy IN, indicating that a concentration driven euphoric effect sought by drug abusers may not be achieved. Due to the higher number of nasal-related AEs, abusers may find DETERx less desirable.
Financial Support: Collegium Pharmaceutical

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A NOVEL BEHAVIORAL ACTIVATION INTERVENTION FOR SMOKING CESSATION; MECHANISMS OF CHANGE.

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Aims: Maintenance of smoking behavior in vulnerable individuals with depressive symptoms is believed to occur through negative and positive reinforcement processes whereby smoking dominates individual's repertoire of behaviors effective in coping with negative affect and obtain rewards. The current study aimed 1) to test the efficacy of a novel behavioral intervention to increase the activation of alternative behaviors while decreasing the smoking behavior in association with negative affect and 2) to investigate its potential mechanisms of change.
Methods: 60 depressed smokers participated in an experimental study. In 4 training sessions, we induced negative affect and manipulated the activation of alternative rewarding behaviors to smoking. Specifically, participants in the experimental condition used a joystick to "push away" smoking related pictures while "pulling toward" pictures related to an alternative rewarding behavior. Such procedure has been used in the past to increase individual's approach motivation. In the control condition, the joystick movement was not contingent on the type of activity. Participants' smoking behavior was assessed during each session as well as one month post intervention. Additionally, the study explored the extent to which the intervention affected the accessibility of the alternative activity and decreased the accessibility of smoking in relation with negative affect.
Results: The results indicate that at one month follow-up, participants in the experimental (vs. control) condition remained abstinent longer while also decreasing the number of cigarettes smoked post relapse. Furthermore, this pattern of results was related to an increase in the accessibility of the alternative activity, but unrelated to the accessibility of smoking.
Conclusions: A short computerized intervention designed to increase individual's motivation to engage in alternative behaviors with rewarding potential can be effective in reducing substance use (i.e. smoking).
Financial Support: NIDA, R01DA018730-06S1

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MOTIVATIONAL ENHANCEMENT, READINESS TO CHANGE, AND TREATMENT SUCCESS IN AFRICAN-AMERICAN SUBSTANCE USERS.

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Aims: Although a body of literature supports the effectiveness of Motivational Enhancement Therapy (MET) in reducing substance use for the general population, several studies report inconsistent findings, especially among African Americans (AA). In the National Drug Abuse Treatment Clinical Trials Network, no overall difference was found between MET and Counseling as Usual (CAU) in the CTN-0004 protocol. Among AA overall, MET showed significantly more days of primary substance use than CAU; however, this pattern was reversed among those with high baseline readiness to change (RTC). We therefore hypothesized a mediator relationship in AA patients, such that (1) MET would positively influence RTC over time and (2) increased RTC would be correlated with successful treatment outcomes.
Methods: We conducted secondary analyses of 194 AA in CTN-0004. RTC was assessed at baseline, 4, 8, and 16 weeks by the University of Rhode Island Change Assessment (URICA), based on precontemplation, contemplation, preparation, and action. Our primary outcome assessed was the total number of days using the primary substance during the 16 week period.
Results: Over the 16 week period, average total RTC score declined slightly, with no significant difference observed between MET and CAU treatment groups. Overall, the MET group reported 6.6 days of primary substance use vs. 3.1 days in the CAU group (p=0.08). We observed an inconsistent role for RTC as a mediator, with RTC change from baseline to 8 weeks significantly associated with substance use in the MET arm (p=0.03), but RTC change to other timepoints not significant. The MET treatment effect was similar in models with and without controlling for baseline RTC and RTC change over time.
Conclusions: These results provide limited evidence for RTC as a mediator of MET effect in AA patients. It is possible that RTC plays a larger role in maintenance of abstinence at the beginning of treatment.
Financial Support: U10 DA013727 (Brady) and U10 DA013732 (Winhusen)

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INITIATING PEOPLE INTO ILLICIT DRUG INJECTION.

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Aims: Although initiation into injection drug use has been studied fairly extensively, few studies have focused on the initiators – that is, people who initiate others into injection. Objective: To examine prevalence of and factors associated with having initiated someone into drug injection ever and in the last 12 months.
Methods: Cross-sectional study of people who inject drugs (PWID; N=605) in California during 2011-2013. Interviews included questions on demographics, drug use and drug injection initiation. We created a composite variable (range 0-3) that included three precursors to initiating others – having injected in front of non-PWID, having described how to inject to non-PWID, and self-reported future likelihood of initiating someone into drug injection. Multivariate logistic regression models identified factors associated with initiating someone ever and in the last 12 months.
Results: The sample was ethnically diverse and over one-quarter female. Thirty-four percent of PWIDs reported having ever initiated someone into injection and 7% had initiated someone in the last 12 months. The following variables were independently associated with having ever initiated someone: being male (Adjusted Odds Ratio [AOR]=1.79; 95% Confidence Interval [CI]=1.04, 3.12), having a high school education or more (AOR=1.74; 95% CI= 1.08, 2.82), having ever been in a gang (AOR=2.11; 95% CI=1.24, 3.60) and scoring two or higher on our precursor to initiation composite score (AOR=5.70; 95% CI=3.51, 9.23). Initiating others in the last 12 months was associated with injecting PWIDs (being a "street doctor") (AOR=3.34; 95% CI= 1.68, 6.67), recent non-injection powder cocaine use (AOR=3.83; 95% CI=1.71, 8.58) and scoring two or higher on our initiation precursor score (6.76; 95% CI=3.21, 14.23).
Conclusions: Our composite measure of precursor to initiation was associated with ever and recent initiation of people into drug injection. Interventions to reduce these behavioral precursors to initiating others into injection are needed.
Financial Support: NIDA grant R01DA027689

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PREVALENCE OF SUBSTANCE USE DISORDERS AND HIV AMONG FEMALE PRISONERS IN UKRAINE.

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Aims: Ukraine has one of the highest incarceration rates in the world, with commercial sex workers and people who inject drugs (PWID) forming a large percentage of incarcerated prisoners. This has led to a concentration of the HIV epidemic within Ukrainian prisons. Since prisons can serve as effective HIV detection and treatment sites, we conducted a comprehensive bio-behavioral health survey among female prisoners in Ukraine.
Methods: Of the 401 women randomly selected for consent from 13 women's prisons in Ukraine, 81 consented to the study and were enrolled in the bio-behavioral and sero-surveillance assessment. Participants underwent pre-test HIV counseling, ACASI and phlebotomy.
Results: Participants (mean age = 34.10 years) reported having had multiple prior arrests (M=3.42, SD=2.73) and multiple prior incarcerations (M=2.1, SD=1.72). Nearly 62% met screening criteria for an AUD, with 16.5% categorized as dependent drinkers according to the AUDIT. Reported drug use in the 30 days prior to arrest was high; nearly 52% reported having used opioids, barbiturates, cocaine, sedatives or hallucinogens and 40% reported poly-drug use. Opioids was the primary drug of choice (48%) followed by amphetamines and sedatives (both 28.4%). Injection drug use (IDU) was also high, with 48% of participants reporting IDU in the 30 days prior to arrest, and disturbingly, 64% reporting re-using a syringe, container, or needle. 23 individuals (28.4%) were diagnosed as being HIV+, of whom nearly a third were newly diagnosed.
Conclusions: The findings from this study provide evidence for the high prevalence of substance use disorders (SUDs), especially IDU, and HIV among female prisoners in Ukraine. A systematic approach towards treatment and linkage to care is needed in Ukraine for HIV+ individuals with co-morbid SUDs who are transitioning to the community.
Financial Support: This research was supported by grants from the National Institute on Drug Abuse for research (R01 DA029910, Altice, PI) and faculty development (K24 DA017072, Altice, PI).

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EFFECT OF MENSTRUAL PHASE AND SOCIAL STRESS ON COGNITIVE PERFORMANCE OF FEMALE MONKEYS.

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Aims: Cognitive function can be affected by fluctuations in ovarian hormones. The goal of this study was to evaluate, in female cynomolgus monkeys, how cognition is affected by hormone fluctuations across the menstrual cycle, and during social hierarchy establishment, which represents a continuum of experiences from environmental enrichment in dominant monkeys to chronic stress in subordinates.
Methods: Monkeys (n=16) were trained on cognitive tasks designed to study executive function and working memory. The acquisition of a simple discrimination (SD) and reversal of discrimination (SDR) task was assessed at four different points of the menstrual cycle, at early/late follicular (LF) and luteal. Subsequently, maintainance of performance was measured over several cycles. Additionally, performance on a delayed matching-to-sample (DMS) task was assessed during the initial week of social hierarchy formation.
Results: Monkeys who acquired the SD task in the LF phase made fewer errors than those other phases. During SDR acquisition, monkeys in the LF phase required fewer trials and made fewer errors and omissions than monkeys in other phases. Subsequent performance did not vary across the menstrual cycle. DMS performance was impaired in future subordinate monkeys during the first week of social hierarchy establishment.
Conclusions: Facilitation in learning a novel task was apparent in the LF phase of the menstrual cycle, but this did not extend into maintainance of performance. This suggests that endogenous hormonal milieu may be more important in the learning of new tasks rather than recall of previously learned ones. The differential effects of social stress on cognition could also reflect hormonal disruptions. Considering the importance of social stress in drug addiction and cognitive approaches in treatment programs, the fact that menstrual phase can profoundly impact acquisition of a task that not even extensive cocaine intake affects in male monkeys, this study adds to our knowledge of the importance of sex difference in the behavioral effects of drugs of abuse.
Financial Support: DA017763, DA29178, DA10584

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PHARMACOGENETICS OF TREATMENT OF OPIOID DEPENDENCE WITH ORAL NALTREXONE AND LONG-ACTING SUSTAINED-RELEASE NALTREXONE IMPLANT.

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Aims: The present study aimed to evaluate the effect variants of the dopamine D2 (DRD2 Ncol) and D4 (DRD4 120 bp) receptor genes, dopamine transporter gene (DAT1 40bp VNTR), mu- (OPRM1 rs510769, rs1799971 (A118G), rs1074287),) and kappa- (OPRK1 rs6473797) opioid receptor genes, and genes of catechol-O-methyltransferase (COMT rs4680) and dopamine beta-hydroxylase [DBH rs1611115 (-1021C/T)] on the tx outcomes of opioid dependence with different drug formulations of naltrexone (oral, implantable and injectable).
Methods: 306 patients with opioid dependence were enrolled into a randomized double blind, double dummy, placebo-controlled, 6-month trial. All participants received drug counseling and either: an implant every 2 months that slowly releases 1000 mg ntx + oral placebo; a placebo implant every 2 months + oral 50 mg oral ntx/day; or placebo implant + oral placebo. All participants provided a blood sample for genetic analysis.
Results: Tx retention and proportion of opiate negative urines were significantly better in the ntx implant group compared to the others. A genotype pattern analysis focusing on the influence of opiate receptor and COMT gene variants on tx retention showed that carriers of the AA-AG-TT or AG-AG-TT genotype patterns of the OPRM1 rs1074287, OPRK1 rs6473797 and COMT genes, and the CC-AG-TT or CT-AG-TT genotype patterns of OPRM1 rs510769, OPRK1 rs6473797and COMT rs4680 had significantly better retention regardless of medication group.
Conclusions: The study showed that genetic analysis is useful for determining potential responders to ntx tx of opioid dependence.
Financial Support: St. Petersburg State Pavlov Medical University
St. Petersburg Bekhterev Research Psychoneurological Institute
National Research Center of Addictions, Russia

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SUSTAINED-RELEASE NALTREXONE FOR OPIOID DEPENDENCE: A COCHRANE REVIEW AND META-ANALYSIS.

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Aims: - Estimate the effectiveness of implantable or injectable sustained release naltrexone in increasing abstinence from illicit opioid use
- Assess and discuss the safety of sustained release naltrexone in opioid dependent patients, including both data-driven and addressing commonly asked topics on safety (e.g. hepatic health, anhedonia/depression, post treatment overdose risk)
Methods: Per-subject urine data was solicited from all RCT authors and subjected to statistical analysis in accordance with Cochrane requirements. Subjective measures of opioid agonist use and other substances were also analyzed. For safety outcomes, a qualitative assessment was conducted of all relevant RCT and non-RCT contributions. Seven databases were searched, producing n=1104 abstracts, of which n=43 were relevant articles and n=6 were RCTs. Risk of bias was assessed for all studies in accordance with Cochrane principles.
Results: Meta-analysis found a main effect of sustained release naltrexone on illicit opioid use ($Z=5.2$, $p<.01$) on both urine and subjective measures. On safety outcomes, sustained release naltrexone was generally well tolerated with some variations in site reactions due to the type of administration method used. Risk of bias was generally considered moderate to high, especially for non-randomized studies.
Conclusions: Sustained release naltrexone increases abstinence from opioids in opioid dependent patients who volunteered for this type of medication-assisted abstinence and was generally safe in use. While no larger studies have yet compared sustained release naltrexone to maintenance treatment with methadone or buprenorphine, this review indicates that sustained release naltrexone can be considered an effective an safe treatment option for opioid dependence. Note: Results & Conclusions are subject to final approval by the Cochrane Drugs & Alcohol Group editorial review board
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PRENATAL INTRAVENOUS NICOTINE EXPOSURE ENHANCES METHAMPHETAMINE SENSITIZATION AND ALTERS BDNF LEVELS IN ADULT RAT OFFSPRING.

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Aims: Prenatal tobacco smoke exposure is associated with increased drug abuse in human populations. The present study examined the effect of low-dose, intravenous (IV) prenatal nicotine (PN) exposure on 1) methamphetamine (METH)-induced locomotor sensitization and 2) brain-derived neurotrophic factor (BDNF) protein levels in rat offspring.
Methods: Pregnant dams received IV nicotine (PN; 0.05 mg/kg) or prenatal saline (PS) 3x/day on gestational days 8-21. In adulthood, offspring received saline or METH (0.3 mg/kg, sc) for 10 days and locomotor activity was tested. Animals received no injections for 14 days prior to testing the expression of METH sensitization. The next day, all animals received saline injections to test context-conditioned activity. After the last locomotor session, the brains from all animals were taken. BDNF levels in the accumbens, striatum, and prefrontal cortex were quantified using ELIZA.
Results: PN rats exhibited greater locomotor activity across 10 days of repeated METH injections compared to PS [$F(1, 72) = 10.0$, $p < .01$]. Expression of METH sensitization [$F(1, 72) = 9.1$, $p < .01$] and METH-induced context-conditioned hyperactivity [$F(1, 72) = 4.8$, $p < .05$] was greater in PN rats relative to controls. PN exposure increased BDNF levels in all regions of the mesocorticolimbic dopamine system relative to PS [$p < .05$ for all regions]. Exposure to repeated METH, however, reduced BDNF levels in the prefrontal cortex [$F(1, 64) = 10.3$, $p < .01$] and striatum in PN rats[$F(1, 64) = 8.1$, $p < .01$]. BDNF protein levels significantly predicted conditioned hyperactivity in PN rats.
Conclusions: PN exposure enhanced the locomotor effects of METH and produced alterations in BDNF levels within the mesocorticolimbic pathway. These findings indicate that PN exposure leads to enduring changes in METH-mediated locomotor behavior and BDNF levels. Together, these data suggest PN alters neural development and may increase drug abuse liability in offspring.
Financial Support: NIDA DA021287

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HCV GENOTYPE DISTRIBUTION AMONG INJECTION DRUG USERS IN TAIWAN.

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Aims: An extremely high prevalence of HCV infection (90%) was detected among injection drug users (IDUs) in Taiwan since 2004. This study aims to better understand the HCV genotype distribution among IDUs in methadone maintenance treatment (MMT) to inform intervention efforts.
Methods: Based on the partial NS5b nucleotide sequence information, the phylogeny and epidemiological profile of 46 HCV strains circulating among 56 IDUs currently in Taiwan's MMT were analyzed. Using genotype classification of HCV as a molecular marker, the origin and the genesis of HCV epidemic were investigated.
Results: The mean age of these participants was 38 ± 7; 74% were male. The phylogenetic analysis showed three direct sequencing viral strains, 1a (31%), 1b (30%) and 6a (26%) genotypes; additionally three cases were identified as 6n, 3b, 2b. The specific 1a cluster was originated in 2004. The monophyletic 1b and 6a clusters were traced back to 2001 and 2002. The transmission rates of these 3 major genotypes were different (6a: 0.057 ± 0.004; 1a: 0.056 ± 0.004; 1b: 0.067 ± 0.005), which indicate potentially different population dynamics in genotype 1b to others.
Conclusions: The HCV genotype distribution among MMT participants in 2013 reflected a different profile compared with the previous published results from 2004 to 2010. These findings suggest there were multiple transmission routes and effects. Future research are needed to identify the specific population dynamics, which can inform needed intervention efforts.
Financial Support: This study was supported by NSC99-2314-B-039-022-MY3 and NHRI-102A1-PDCO-1312141.

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DISORDERED EATING AND SUBSTANCE USE: FINDINGS FROM A NATIONAL SAMPLE OF ADOLESCENTS.

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Aims: The co-morbidity of substance use and eating disorders has been a robust finding in the literature; however limited research has investigated the role of disordered eating behaviors in a non-clinical sample of adolescents (Harrop & Marlatt, 2010). Given the high co-morbidity of disordered eating and substance use, the current study sought to examine the relationship of the use of diet pills, vomiting or laxative use, and fasting and the use of substances (cigarettes, alcohol, marijuana, and cocaine) in the past thirty days, in national sample of adolescents who completed the Youth Risk Behavior Survey (N = 15,364). Previous research has shown a relationship between disordered eating and substance use; however, potential changes in the relationship of these factors have not been investigated (Pisetsky et al., 2008). Following the findings of previous research, it was hypothesized that all three disordered eating behaviors would significantly predict greater substance use.
Methods: Regression analyses were used to determine the relationship of disordered eating behaviors and substance use.
Results: When investigating this relationship, diet pills use significantly predicted greater use of substances in the last 30 days for: binge drinking ($p<0.001$), cigarettes ($p=0.001$), marijuana ($p=0.002$), and cocaine ($p<0.001$). Engaging in fasting behaviors predicted significantly greater use of cigarettes in the past 30 days ($p<0.001$), binge drinking in the past 30 days ($p<0.001$), cocaine use in the past 30 days ($p=0.01$), and marijuana use in the past 30 days ($p<0.001$). Finally, vomiting or laxative use for weight loss predicted significant more days smoking in the past 30 days ($p<0.001$), binge drinking in the past 30 days ($p<0.001$), cocaine use in the past 30 days ($p<0.001$), and marijuana use in the past 30 days ($p<0.001$).
Conclusions: All dieting behaviors significantly predicted greater use of alcohol, cigarettes, cocaine, and marijuana in the past 30 days. Gender differences in this relationship will be investigated, and the implications of these findings for practice and theory will be discussed.
Financial Support: No financial support was received for this study.

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PREFRONTAL AND STRIATAL FMRI RESPONSE PREDICTS ADHERENCE TO INJECTABLE EXTENDED-RELEASE NALTREXONE IN OPIOID DEPENDENCE.

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Aims: This ongoing study is testing the hypothesis that prefrontal and limbic response to drug-related visual cues may predict adherence to injectable extended-release naltrexone (XR-NTX) treatment in prescription opioid dependent (POP) patients.
Methods: Twenty-four POP participants (4F) received up to 3 monthly XR-NXT injections. After detoxification and before the first XR-NTX injection, functional Magnetic Resonance Imaging (fMRI) of the brain was performed. During fMRI, participants viewed a sequence of heroin-related images (cues) and control images. Other variables included changes in drug craving and plasma levels of naltrexone and 6-beta-naltrexol at three time-points during the XR-NTX. Individual fMRI data were analyzed using standard procedures in FSL. Whole brain comparison was carried out to compare the brain response to heroin-related cues in participants who completed the study (i.e. received 3 XR-NTX injections) and those who dropped out.
Results: In this ongoing project, 14 participants completed the study and 10 dropped out after zero to 2 XR-NTX injections. In the PRE_XRNT session, participants who later dropped out of the study (N=10), showed greater response to heroin cues ($z \geq 2.1$, uncorrected) in the bilateral inferior frontal, medial frontal and anterior cingulate gyri and bilateral ventral striatum, than the participants who completed the study.
Conclusions: These evolving data suggest, that brain response to drug-related cues may predict adherence to treatment in prescription opioid dependent patients.
Financial Support: A CURE Addiction Center of Excellence SAP#4100055577, R03 DA035683-01, Analytical Services Program of the NIH and the Veterans Administration. Study medication (XR-NTX, Vivitrol®) was provided by Alkermes Inc. through Investigator-Sponsored Study (ISS) grant.

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EFFECTS OF ANATABINE AT RELEVANT HUMAN NICOTINIC RECEPTOR SUBTYPES IN VITRO AND ON CRAVING AND C-REACTIVE PROTEIN IN HEAVY SMOKERS.

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Aims: Anatabine is a *Solanaceae* plant family alkaloid structurally similar to nicotine. It has no discernable abuse potential and attenuates nicotine's interoceptive and reinforcing effects in animals. Studies in humans show that anatabine reduces acute cigarette craving. Anatabine also has anti-inflammatory effects in vitro and in vivo. We evaluated anatabine's effects at relevant nicotinic receptor (nAChR) subtypes in vitro and on craving and the systemic inflammatory biomarker C-reactive protein (CRP) in heavy smokers.
Methods: In vitro: Functional receptor binding assays evaluated anatabine's effects at $\alpha4\beta2$, $\alpha3\beta4$, and $\alpha7$ cloned human nAChR subtypes in mammalian cells. Human: Heavy smokers (≥1 pack per day for ≥5 years) took two 1-mg oral anatabine lozenges three times per day for two weeks. Repeated assessments included safety, the Questionnaire on Smoking Urges (QSU), the Minnesota Withdrawal Behavior Rating Scale (MBRS), and serum CRP.
Results: In vitro: Anatabine was a full agonist at $\alpha4\beta2$ and $\alpha7$, and a partial agonist at $\alpha3\beta4$. Relative to nicotine, anatabine was much less potent at $\alpha4\beta2$, and had similar potency at $\alpha3\beta4$ and $\alpha7$. Human: After two weeks of anatabine supplementation, subjects reported significant ($p<0.0001$) reductions from baseline in QSU and MBRS scores. Subjects with blood levels of anatabine >12 ng/mL had CRP levels about 30% lower than those with anatabine levels ≤12 ng/mL ($p<0.02$). The anatabine supplement was safe and well tolerated.
Conclusions: The effects of anatabine on nicotine reinforcement and craving in animal and human studies, respectively, and on inflammatory biomarkers such as CRP may be mediated through activity at $\alpha4\beta2$, $\alpha3\beta4$, and $\alpha7$ nAChR subtypes. Anatabine shows promise as a candidate for further study as a means of reducing the urge to smoke or use tobacco products, and as an anti-inflammatory supplement with a novel mechanism of action.
Financial Support: This work was funded by Rock Creek Pharmaceuticals, Inc., Gloucester, MA.

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MEDICAL MARIJUANA: STEPPING STONE OR PROTECTIVE EFFECT?

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Aims: Following implementation of medical marijuana laws around the U.S., concerns have been raised that greater availability and acceptance of marijuana could be associated with increased use of illicit drugs among young adults, which follows the logic of the stepping stone theory. However, other research suggests that regular access to marijuana through medical marijuana programs may offer a protective effect against initiating other drugs.
Methods: A total of 301 young adults (18-25 years old) were recruited in Los Angeles between 2009-11 as part of a study focusing on prescription drug misuse. Among the sample, 56 (18.6%) reported being a current medical marijuana patient (MMP) compared to 245 (81.4%) who were non-patient users (NPU) of marijuana. Participants were administered a cross-sectional survey and answered a range of questions pertaining to history of marijuana use, illicit drug use, and prescription drug misuse.
Results: First, a "maturing out" process occurred among NPU: fewer members of the oldest cohort used marijuana in the past 90 days compared to the youngest cohorts (48.7% vs. 67.8%). In contrast, no maturing out process occurred among MMP: each age cohort reported nearly identical marijuana use (approximately 80% reported use of marijuana in the past 90 days). Overall, a greater proportion of MMP reported 90 day use of marijuana compared to NPU (80.2% vs. 64%). Second, a significantly smaller proportion of MMP reported lifetime use of three key illicit drugs compared to NPU: ecstasy (75% vs. 87.3%); cocaine (67.9% vs. 83.7%); and methamphetamine (48.2 vs. 64.5%). Also, a lower proportion of MMP reported lifetime misuse of OxyContin and Xanax compared to NPU (but not statistically significant)
Conclusions: Among MMP in this study, a greater proportion were recent marijuana users and a lower proportion were lifetime users of illicit and prescription drugs. Among NPU, the reverse was true. Overall, these findings provide preliminary evidence to suggest that among young MMP, marijuana could provide a protective effect against initiating illicit and prescription drugs.
Financial Support: Grant support was provided by the NIDA (DA021299).

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OPIOID SUBSTITUTION THERAPY AS A STRATEGY TO REDUCE DEATHS IN PRISON: RETROSPECTIVE COHORT STUDY.

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Aims: To describe deaths in prison in a cohort of opioid-dependent people, and examine associations between receipt of opioid substitution therapy (OST) and risk of death while in prison.
Methods: We linked state-wide OST data to incarceration and mortality data. We calculated crude mortality rates (CMR) for all-cause and unnatural (suicide, drug-induced, violent and injury) deaths in prison, and used Cox regression to assess adjusted associations between death and receipt of OST. Rates and hazard ratios were calculated for the entirety of time in prison, and for the first four weeks in prison.
Results: The cohort comprised 16,715 opioid-dependent people who had been incarcerated. Fifty-one people died in prison. Compared to periods of time in OST, all-cause and unnatural mortality rates were significantly higher while not in OST (all-cause rate ratio (RR): 4.1; 95% confidence interval (CI): 2.1, 8.0; unnatural death RR: 6.7; 95% CI: 2.6, 17.3). Compared to time out of OST, the hazard of all-cause death was 74% lower while in OST (adjusted hazard ratio (AHR): 0.26; 95% CI: 0.13, 0.50), and the hazard of unnatural death was 87% lower while in OST (AHR: 0.13; 95% CI: 0.05, 0.35). In the first four weeks of incarceration, compared to periods in OST, all-cause mortality was 16.6 (95% CI: 2.2, 124.9) times higher, and unnatural mortality was 14.0 (95% CI: 1.8, 107.9) times higher when not in OST. Compared to periods not in OST, the hazard of all-cause death during the first 4 weeks of incarceration was 94% lower while in OST (AHR: 0.06; 95% CI: 0.01, 0.48), and the hazard of unnatural death was 93% lower while in OST (AHR: 0.07; 95% CI: 0.01, 0.53).
Conclusions: Ensuring a high coverage of OST in correctional facilities will help to minimize deaths, particularly unnatural deaths, among opioid-dependent prisoners. Timely access to OST while incarcerated is critical to realizing this benefit.
Financial Support: National Health and Medical Research Council

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COGNITIVE BIAS MODIFICATION COMBINED WITH COGNITIVE BEHAVIORAL THERAPY: A SMOKING CESSATION INTERVENTION FOR ADOLESCENTS.

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Aims: Recent intervention studies on adolescent smoking cessation indicate that cognitive behavioural therapy (i.e., CBT) is less efficient among impulsive adolescents. Existing evidence suggests that retraining relatively automatic impulsive action tendencies using cognitive bias modification (i.e., CBM) increased treatment outcome (i.e., alcohol relapse). Given these findings, we conducted a pilot trial to examine if combining CBT with CBM improved smoking cessation outcomes among adolescents. We hypothesized improved treatment outcome when adolescents received both CBT and CBM compared with CBT only.
Methods: The study was conducted in the United States and the Netherlands. Adolescent smokers (N=60; 18 in US, 42 in Netherlands) participated in a 4-week smoking cessation program combining weekly CBT with CBM to avoid smoking stimuli or a placebo condition with no training. Treatment outcome: 7 day point prevalence abstinence determined using self-reports validated by cotinine levels at the end of treatment (i.e., EOT).
Results: Repeated-measure ANOVA showed that at EOT, adolescents in the CBM condition had an avoidance bias whereas those in the placebo condition had an approach bias. We did not observe enhanced treatment outcomes in the CBM compared with placebo condition. However, exploratory analyses that included only participants completing all training sessions indicated that participants in the CBM condition had reduced cotinine levels whereas those in the placebo condition had not in the Dutch sample but not in the total sample.
Conclusions: Generally, intent-to-treat analysis demonstrates no increase in smoking cessation in the CBM condition. Retraining automatic behavioral tendencies may only improve smoking cessation outcomes in highly motivated adolescents who are willing to complete all training sessions.
Financial Support: NIDA, ZonMW

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PREDICTORS OF POSITIVE DRUG SCREENS AFTER DEPLOYMENT TO IRAQ OR AFGHANISTAN IN THE MILITARY DRUG TESTING PROGRAM.

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Aims: Problems associated with alcohol and drug use remain a critical area for intervention development within the Department of Defense (DoD). While there is routine postdeployment screening, drug problems area not documented. This study identifies predictors of testing positive for one or more drugs postdeployment among 306,345 enlisted Army active duty (AD) members returning from Iraq or Afghanistan in FY2008-2011.
Methods: Urinalysis tests for cocaine, heroin, THC, amphetamines, and/or designer amphetamines, routinely tested by the DoD, were examined to estimate the percent of the sample with any positive drug test 6-month to 3-year postdeployment (followup). Demographic and deployment characteristics were examined as potential predictors of a positive drug screen. Multivariate models controlled for study design variables (number of tests, last collection date relative to deployment end).
Results: Of AD enlisted members, >80% with urinalysis data were analyzed. Most had at least one random test (median 4) during followup. An estimated 2.74%, 95% confidence interval CI: 2.68-2.89% tested positive. Controlling for design, demographics, and deployment characteristics, with increased odds of a positive drug screen were combat specialist occupation (relative to 4 other groups), in early cohort (deployment began before FY2011), short deployment (relative to 1 year, or >1 year), first deployment (prior deployment ended >365 days before index), and assigned to a Warrior Transition Unit (WTU, rather than regular military duties) upon return.
Conclusions: Preliminary findings suggest that combat specialist occupations and first deployers were most at risk. Two measures which may be proxies for returning wounded also had increased odds of a positive drug test. Knowledge of these characteristics may help target new strategies or interventions such as additional screening or brief counseling.
Financial Support: NIDA R01DA030150

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GENDER DIFFERENCES IN RISK FACTORS FOR NONMEDICAL USE OF PRESCRIPTION STIMULANTS AMONG YOUTH 10 TO 18 YEARS IN THE U.S.

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Aims: Nonmedical use of prescription stimulants (NMU) is a significant public health concern with increased risk among adolescent girls. Given the complex and multiple pathways that contribute to drug use, this study examines gender differences and gender specific associations of NMU across domains.
Methods: Data comes from the National Monitoring of Prescription Stimulants Study (NMAPSS) which surveyed 11048 10 to 18 year olds via an entertainment venue intercept recruitment method. NMU was defined as using prescription stimulants more than prescribed, stimulants that belonged to someone else, by non-oral routes, or use to get high. Photos of pills were used to ensure proper recall. Variables examined included those in the socio-demographic, psychological and peer domains.
Results: Among the 3.6% of youth reporting past 30 day NMU, 46% were girls. Among youth with NMU, depression (54% vs. 46%), anxiety (57% vs. 43%) and weight concerns (72% vs.28%) were significantly higher in girls than boys, though boys had higher rates of ADHD (62% vs. 38%) and conduct problems (66% vs. 34%). Multivariable logistic regression indicated that girls with ADHD (OR 1.65), weight concerns (OR 3.38), and those who smoked (OR 2.48), or reported illegal drug use (OR 4.87) or had a friend who used stimulants (OR 6.53) were more likely than those without to report NMU. Among boys, increased odds of NMU were found for alcohol use (OR 2.24), illegal drugs (OR 3.25) or having a friend who used stimulants (OR 6.61).
Conclusions: General and specific risk factors based on gender are associated with NMU across demographic, psychological and peer domains. The implications of gender differences in vulnerability to NMU pertain to the design of targeted prevention and interventions programs.
Financial Support: Fogarty International Centre Indo-US Training Program in Non-Communicable Diseases (Grant No D 43-TW009120; Sonam O Lasopa, Fellow; PI: Cottler).
NMAPSS was conducted under contract from Pinney Associates, Inc. Pinney is provided funding by Shire Pharmaceutical and Noven Pharmaceuticals.

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IMPAIRED EXECUTIVE FUNCTION, DRUG AND SEX RISK, AND HIV INFECTION IN AFRICAN-AMERICAN MEN.

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Aims: To determine if impaired planning, an executive function measured by the Tower of London (TOL) neuropsychological assessment, contributes to drug and sex risk, and, in turn, HIV infection in a population of African American men.
Methods: Using data collected during the baseline visit of the Neuro-HIV Intervention Study (N=244), we estimated adjusted prevalence ratios (APRs) and 95% confidence intervals (CIs) for associations between impaired planning and problem solving ability, defined as having a TOL standardized total excess moves score below the 10th percentile, and outcomes including risky injection practices (ever having shared needles, cookers, cotton, or rinse water and ever having backloaded), binge drinking, sexual risk behaviors (casual sex, buying sex), and biologically-confirmed HIV infection.
Results: Approximately 18% were HIV-infected. In analyses adjusting for age and education, impairment on TOL was significantly associated with HIV infection (APR: 1.81, 95% CI: 1.09, 3.01) and with potential mediating behavioral factors including needle sharing (APR: 1.69, 95% CI: 1.03-2.73), binge drinking (APR: 2.03, 95% CI: 1.13, 3.24), and buying sex (APR: 2.50, 95% CI: 1.66, 3.78). However, when adjusting for these hypothesized causal intermediates, the APR between TOL and HIV strengthened (APR: 2.01, 95% CI: 1.21, 3.33), suggesting other factors mediate the association between impaired planning and problem solving and HIV infection.
Conclusions: Impaired planning and problem solving ability is associated with HIV infection among African American men, suggesting that interventions designed to improve these executive functions may reduce HIV infection in this population. However, to best plan interventions to address improved planning to reduce behavioral risk that drive HIV, additional research is needed to identify the behavioral determinants of HIV infection that are most strongly influenced by impaired executive function.
Financial Support: R01DA14498

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RESULTS FROM THE FIRST NATIONWIDE SURVEY OF STUDENTS IN COLLEGIATE RECOVERY PROGRAMS.

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Aims: Substance use disorders (SUD) often start in adolescence, making this transitional period critical. Treatment is effective for youths but relapse is common. For youths in SUD remission wishing to attend college, the high rates of substance use on campus are a serious threat to continued sobriety. Collegiate Recovery Programs (CRPs) are an innovative model of campus-based recovery support that is growing exponentially but remains unexplored. Demographic and clinical information is lacking on students in CRPs and on their experiences with CRPs. Such knowledge can inform model development and evaluation.
Methods: Data from an online survey of CRP students describes their background and clinical history, reasons for CRP participation, overall experiences with and use of CRP services.
Results: Students (preliminary N = 480, target M = 550) from 25 universities in17 states were 56% male, Caucasians (91%) with an average age of 26; 12% were veterans. Drugs had been the primary problem for 58% (42% alcohol). Over half (59%) had been charged with a crime and 33% had had a period of homelessness; 82% had been in addiction treatment, 93% had attended 12-steps. Although substance-free, a minority engage in other addictive behaviors at a problematic level (e.g., 12% each compulsive eating and sex/love addiction past 90 days); 41% smoke and 66% are being treated for a mental health problem. CRP enrollment duration ranged from 1 to 8 semesters; top referral sources are word of mouth (29%), treatment (22%) and 12-step groups (12%). One third of students said they would not be in college right now were it not for the CRP and 60% find the CRP quite a bit or extremely helpful to their recovery.
Conclusions: CRP students experienced severe consequences of their SUD; CRPs may promote college attendance in recovery. Further information is needed on compulsive behavior patterns in recovery to promote healthy functioning.
Financial Support: Financial support NIDA Grant # R21DA033448

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REPORTED USE OF NON-PRESCRIBED MARIJUANA FOR BIOMEDICAL AND PSYCHIATRIC CONDITIONS AMONG REGULAR MARIJUANA USERS.

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Aims: A growing body of literature has examined the use of medical marijuana to treat a variety of biomedical and psychiatric conditions. Given emerging scientific evidence supporting the benefits of medical marijuana, it is possible that people consume this substance to self-medicate regardless of prescription status. Therefore, we evaluated the types of biomedical and psychiatric conditions for which regular users of this substance report consuming marijuana without a prescription.
Methods: We recruited 513 respondents as part of a larger web-based study examining the psychometric properties of a questionnaire assessing self-efficacy to reduce marijuana use. Of these, 169 provided codeable responses to the open-ended question: "If you use marijuana for medical purposes but do not currently have a prescription for its use, what health condition(s) are you using it for?"
Results: The most common biomedical conditions for which respondents reported self-medicating with marijuana were insomnia (n = 64), pain (n = 39), nausea/appetite stimulation (n = 22), and headaches (n = 21). The most commonly reported psychiatric conditions were anxiety (n = 71), depression (n = 44), and attention problems (n = 7). Overall, we found that there were approximately as many reports of use of marijuana for psychiatric conditions as there were reports of use for biomedical conditions.
Conclusions: These findings suggest that a substantial subset of marijuana users report using marijuana without a prescription to treat a variety of biomedical and psychiatric conditions. Limitations of this study include extrapolating from a relatively small convenience sample and use of open-ended questions, which assumes that respondents have the ability to describe their experiences accurately. Further research in this area is warranted in order to inform current and impending legislation and to explore the prevalence, effectiveness, harms and benefits, and clinical implications of self-medication using marijuana.
Financial Support: None

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CHILDCARE IN FAMILIES WITH SUD MOTHERS OR FATHERS.

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Aims: Care for children is often compromised in mothers with substance use disorders and contribute to risk for negative child outcomes (e.g., Staton-Tindall et al., 2013). In the present study we examined reports of childcare in two-parent families. We hypothesized that mothers, over fathers, would act as primary caregivers regardless of which parent had SUD.
Methods: Participants were 72 couples in which the father (n = 56) or mother (n = 16) met criteria for SUD. On average, parents were in their 30s, had a high school education, and low-to-middle income. Mean child age was 9.58 (SD = 4.81). Parents' caregiving was assessed over the previous three months. Common childcare items were scored as: 1) I usually do, 2) my partner and I share equally, or 3) my partner usually does. Parents also rated responsibility for day-to-day care of their child from: 1) I have total responsibility, to 5) My partner has total responsibility.
Results: In SUD mother families, mothers were still significantly more likely to be responsible for all aspects of childcare (i.e., the mother was more likely to stay home with a sick child [$t(15) = 2.51$, $p = .025$)], go to doctor's appointments/teachers' meetings, [$t(15) = 3.30$, $p = .005$)], arrange for childcare [$t(15) = 4.95$, $p < .001$)], and plan day-to-day activities [$t(15) = 3.65$, $p = .002$]. In SUD mother families, parents were equally likely to transport the child and report being responsible for child supervision. In SUD father families, with one exception (i.e., stays home when child is sick), mothers were significantly more likely to be responsible for childcare (all ps <.001).
Conclusions: Responsibility for childcare appears to fall to the mother, regardless of which parent has SUD. This finding has important implications for efficacy of interventions aimed at improving caregiving for children who reside with a substance-abusing parent.
Financial Support: This work was supported by the National Institute of Drug Abuse (R01-DA024740; PI: Kelley).

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WITHDRAWN

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SMOKERS IN ADDICTION TREATMENT SEE THEIR RISK OF TOBACCO-RELATED DISEASE AS LOWER THAN THAT OF AN AVERAGE SMOKER.

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Aims: A number of studies have assessed smoking risk perception in the general population, but few have assessed perceived risk among persons in addiction treatment. This is of interest because smoking prevalence in addiction treatment settings is 3-4 times that in the general population. We examined smoking risk perception among smokers in addiction treatment programs.
Methods: 376 clients from 8 addiction treatment programs in New York were surveyed from May to September 2013. Participants were asked to estimate health risks for themselves and for an average smoker defined by scenarios. On the scale of 0% to 100%, they were asked to evaluate the risks of getting lung cancer, bad cough, having trouble breathing, heart attack, and mouth/lip cancer. Paired t tests were used to compare how they estimated their own health risks and how they estimated the health risks of the average smoker.
Results: 67% participants (n = 252) were current smokers. Smokers consistently estimated their own risks from tobacco as lower than those of the average smoker: lung cancer (57.2% vs. 61.6%, p = 0.005), bad cough (60.4% vs. 67.4%, p < 0.001), trouble catching breath (64.5% vs. 70.0%, p=0.001), mouth/lip cancer (47.1% vs. 55.6%, p<0.001), and heart attack (57.4% vs. 63.4%, p<0.001). Level of risks that smokers estimated for themselves was not correlated with the number of cigarettes smoked per day (CPD) for lung or mouth cancer, and weakly correlated for bad cough (r=0.16, p=0.018), trouble breathing (r=0.19, p=0.005), and heart attack (r=0.20, p=0.003).
Conclusions: While smokers enrolled in addiction treatment programs may overestimate risk of lung and mouth cancer, they perceived lower tobacco-related health risks in themselves as compared to an average smoker. Self-perceived risk was only weakly associated, with CPD. Improving accurate perception of tobacco-related health risks among person in addiction treatment may increase acceptance of tobacco restrictions and use of tobacco cessation services.
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THE STREET PRICES OF IMMEDIATE- AND EXTENDED-RELEASE TAPENTADOL ARE LOWER THAN OTHER SCHEDULE II OPIOID TABLETS/CAPSULES.

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Aims: Tapentadol [Nucynta®] is a US DEA Schedule II analgesic with dual actions: mu agonist activity and norepinephrine reuptake inhibition. This analysis compares street prices of immediate release (IR) and extended release (ER) tapentadol to other Schedule II opioid tablets/capsules using data from the RADARS® System StreetRx Program.
Methods: StreetRx is a website that enables real-time collection, organization and display of street price data on diverted pharmaceutical products. Site users anonymously submit prices they paid or heard were paid for diverted prescription drugs. The median street price per milligram (mg) from reports submitted between 3rd quarter 2011 to 2nd quarter 2013 for ER tapentadol, IR tapentadol, and other Schedule II opioid tablets/capsules were calculated. Geometric mean street price per mg of tapentadol was compared to other Schedule II opioid tablets/capsules.
Results: There were 24 reports of IR tapentadol, 3 reports of ER tapentadol, and 1,172 reports of other Schedule II opioid tablets/capsules. The median street price per mg was $0.20 for IR tapentadol, $0.10 for ER tapentadol, and $1.00 Other Schedule II opioid tablets. The geometric mean of other Schedule II opioid tablets/capsules ($0.98, 95% CI: $0.93-$1.04) was 6.4 (95% CI: 4.5-9.2, p<0.001) times greater than the geometric mean of tapentadol products ($0.15, 95% CI: $0.11-$0.22).
Conclusions: The number of reports and average street price per mg of tapentadol suggest that the demand for diverted tapentadol since 3rd quarter of 2011 is low compared to other Schedule II products. Continued surveillance of tapentadol is needed to determine whether these findings persist with the continued changes to opioid products.
Financial Support: The RADARS® System is part of Denver Health and Hospital Authority, a division of the state of Colorado. It is supported by subscriptions from pharmaceutical manufacturers.

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INTERLEUKIN-1β IN THE DORSAL HIPPOCAMPUS AND THE CONDITIONED IMMUNE EFFECTS OF HEROIN.

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Aims: Heroin suppresses the immune system and exposure to environments associated with heroin use can also produce immunosuppression. The dorsal hippocampus (DH) is necessary for this learned effect. IL-1β is a pro-inflammatory cytokine linked to learning and memory and is expressed within the DH. Present studies investigated the role of DH IL-1β in heroin conditioned immunosuppression and food conditioned place preference (CPP).
Methods: Rats were DH cannulated and conditioned to associate heroin's unconditioned effects with a context (5 pairings). They were then microinjected with IL-1β siRNA or missense control siRNA prior to either re-exposure to the heroin-paired context or return to the home cage. Immediately afterward, the immune system was challenged with lipopolysaccharide (LPS). Rats were sacrificed 6-hrs later. Spleenic iNOS was assessed by real-time qRT-PCR and plasma nitrate/nitrite levels in by Greiss Reagent Assay. CPP was established in another cohort of DH cannulated rats by pairing food with one context. Rats were injected with IL-1β siRNA or missense control siRNA prior to testing for CPP again.
Results: IL-1β siRNA prevented the heroin context's ability to suppress the normal splenic induction of iNOS ($p<0.05$) and plasma nitrate/nitrite ($p<0.05$) after immune challenge. Most importantly, we showed that the same IL-1β manipulation did not alter food-associated memory in a conditioned place preference paradigm ($p>0.05$), indicating that IL-1β suppression did not disrupt memory in general, but is more specifically linked to heroin.
Conclusions: These studies reveal what could be a drug-memory specific mechanism that distinguishes the drug responses from normal natural reward responding. Understanding this conditioned effect will critically inform our knowledge of how these associations engage memory and immune systems and possibly provide therapeutic targets to help restore immune function in drug users.
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ASAM TREATMENT PLACEMENT CRITERIA FOR GAMBLING DISORDER.

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Aims: Gambling disorder (GD) is placed in DSM 5 under the category Substance Related and Addictive Disorders. American Society for Addiction Medicine (ASAM) guidelines for treatment placement are relevant for recommending gamblers to the appropriate level of care, but they are rarely used in GD. The aims of the present study were to: adapt ASAM placement criteria to individuals with GD receiving outpatient treatment; and determine how many patients are appropriate for and willing to accept referrals to higher care levels.
Methods: Therapists and their patients receiving treatment for GD participated. Therapists assessed ASAM placement criteria for each of their patients. Therapists also asked their patients to complete a questionnaire that assessed GD severity and factors corresponding to ASAM criteria for residential and intensive outpatient (IOP) care. Therapists and clients completed and mailed their questionnaires to our offices. Therapists (N=26) completed and returned checklists on 125 patients, and 76 patients returned their questionnaires.
Results: Therapists recommended residential treatment for 15% of cases, and recommended IOP for 20%. Recommendations were associated with ASAM ratings: treatment failure, co-occurring pathology, impulsivity, suicide risk, self-destructive behavior, mental and physical exhaustion and strong urges to gamble. Over 43% of patients indicated high willingness to attend residential treatment and half indicated willingness to attend IOP. Willingness to attend was associated with greater overall difficulty in psychiatric functioning. There was good agreement between therapist and patient ratings on appropriate level of care as well as correspondence between patient willingness and therapist ratings of ASAM-based level of pathology.
Conclusions: These data demonstrate that patient placement criteria designed for substance users can be applied to problem gamblers to determine appropriate level of care.
Financial Support: Michigan Department of Community Health and Helene Lycacki/Joe Young, Sr. Funds (Michigan)

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A COMPARISON OF TEMPORAL DISCOUNTING IN ADOLESCENTS AND ADULTS IN TREATMENT FOR CANNABIS USE DISORDERS.

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Aims: Temporal discounting is a predictor of poor treatment outcomes in adolescents and adults with cannabis use disorders (CUD), and is modestly associated with heavier cannabis use and dependence. However, no study has examined whether discounting rates differ between adolescent and adult cannabis users. The aim of the current study was to compare temporal discounting rates between adolescent and adult cannabis users enrolled in treatment for CUD in order to determine whether baseline and/or pre- to post- treatment changes in discounting rates differ between age groups.
Methods: Participants were 174 adolescents and 128 adults enrolled in clinical studies examining behavioral treatments for CUD. Participants completed a temporal discounting task at baseline, end of treatment and at 6 months post-treatment for two commodities (money and cannabis) at two different magnitudes ($100 and $1000). Repeated measures mixed models examined baseline differences in commodity and magnitude across age groups, and changes in discounting at each commodity and magnitude from pre- to post- treatment.
Results: At baseline, magnitude and age interacted ($p<.001$) with only adults showing greater discounting of $100 compared to $1000 across commodities. Commodity and age interacted ($p<.001$) with adolescents discounting money more than adults. Discounting rates decreased from pre- to post- treatment ($p<.001$), and with greater decreases in discounting of cannabis ($p<.001$). Adults had significantly greater decreases in cannabis discounting over the course of treatment relative to adolescents ($p<.05$).
Conclusions: Relative to adults, adolescents are less sensitive to changes in magnitude of rewards, discount money at higher rates and show less improvement in discounting over the course of treatment. Comparing temporal discounting in adolescents and adults with CUD is important to better understand how development influences the impact of impulsive decision-making on substance use and its treatment.
Financial Support: NIDA R01-DA015186 and R01-DA023526

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SEX-DIFFERENCES IN COGNITION AND BEHAVIORS IN CHILDREN WITH FAMILY HISTORY OF SUBSTANCE USE DISORDERS.

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Aims: Substance use disorder (SUD) is highly heritable, but it is unclear whether SUD-related cognitive and behavioral deficits are inherited and if they are sexually dimorphic. Polymorphisms in catechol-O-methyltransferase (COMT) genes have been associated with sex-specific deficits associated with SUD. The aim is to determine the association between two COMT genotype variants, sex, and family history of SUD (FSUD) on behavioral measures and cognition in typically developing children.
Methods: FSUD, externalizing behavior and total ADHD scores were reported by parents of 226 children ages 3-20 years (85 SUD: 10.1±0.5 years, 48 boys; 141 CON: 10.0±0.4 years, 74 boys). Cognitive performance was assessed by full scale IQ (FSIQ) and the NIH Toolbox®. Saliva samples were genotyped for two functional COMT single nucleotide polymorphisms (SNPs): rs4680 (Val158Met) and rs165599 (near the 3′UTR region).
Results: On 3-way (SNP, sex, FSUD) ANOVAs, rs165599 tended to have negative effects on ADHD scores (p=0.08) and externalizing behaviors (p=0.06), with male AA-carriers with FSUD having higher ADHD scores (p=0.10) and externalizing behaviors (p=0.03). COMT rs165599 variant tended to have a negative effect on FSIQ (p=0.08) and IQ processing speed (p=0.07), with male AA-carriers with FSUD having the lowest scores. Regardless of FSUD, males with the rs4680 variant tended to have lower FSIQ (p=0.06), but significantly lower processing speed scores (p=0.003).
Conclusions: The COMT genetic variants appear to have a greater negative influence on boys. FSUD boys with the rs165599 AA-genotype had greater ADHD symptoms and externalizing behaviors as well as lower FSIQ and slower processing speed. Both behaviors and cognitive function may be influenced by these genes involved in dopamine metabolism in a sex-specific manner.
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IMPLEMENTATION OF DRUG AND HIV RISK COUNSELING IN MMT PROGRAMS IN TAIWAN.

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Aims: Few methadone maintenance treatment (MMT) programs in Taiwan offer drug counseling and data on program implementation have rarely been reported. This study aims to examine the feasibility of Behavioral Drug and Risk Counseling (BDRC) as a component of MMTP and documents its implementation in Taiwan.
Methods: 90 MMT patients were randomly assigned to treatment as usual (n=45, MMT only) or MMT+BDRC (n=45). Patients in the BDRC group receive weekly counseling in the first month, bi-weekly in months 2 and 3, and monthly in months 4 to 7 after enrollment. BDRC sessions offer education on biological and pharmacological mechanisms of heroin and methadone, skills to reduce/avoid HIV risk behaviors, maintaining or improving medication adherence, and establishing non-drug related activities supporting recovery. BDRC utilizes health education, setting small and achievable goals, positive feedback, and developing plans and skills to improve treatment participation and prolonged drug recovery. BDRC counselors (n=4) received a 5-day training workshop at the program onset. Clinical supervision, including case discussions, is conducted monthly and lead by an experienced psychotherapist. Counselors maintain content checklists and notes from each session.
Results: Content analysis of the checklists and counseling notes showed that counselors were able to deliver the BDRC but fidelity of counseling intervention varies between sites and counselors. Factors influencing intervention fidelity include: counselor's professional background and past training, and site/organizational characteristics (e.g., availability of separate and confidential counseling space, coordination between case managers and counselors) and frequency of clinical supervision.
Conclusions: Our preliminary findings support the potential of integrating behavioral counseling into regular MMT as a component of a comprehensive treatment in Taiwan.
Financial Support: Supported by National Science Council (NSC100-2628-H-003-002-MY3)

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WHAT PREDICTS CONTINUED SUBSTANCE USE AMONG PROBATIONERS?

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Aims: Probation supervision is designed to motivate drug users to suppress illicit substance use during supervision. The probation suppression effect has not been adequately tested. This study examines predictors of continued illicit substance use among probationers in two urban areas.
Methods: 142 substance-using probationers participating in an ongoing randomized control trial. Probationers completed baseline and 2-month follow-up (2MFU) interviews. Probationers averaged 37 years old and were predominately male (72.5%) and African-American (68.9%). The measures examined include age, criminal justice (e.g., lifetime arrests), treatment/use (e.g., recent hard drug use), and psychosocial (e.g., problem recognition) factors. Hard drug use includes opiates, cocaine, barbiturates, amphetamines, hallucinogens, and inhalants, which are statistically significant independent predictors of criminal behavior. Bivariate correlations and logistic regression models examined the relationship between individual factors and continued drug use (any) and hard drug use.
Results: Bivariate analysis revealed homelessness, recent poly-substance use, recent hard drug use, substance use with family members, and peer substance use were associated with 2MFU overall drug use. Prior substance abuse treatment, age of first drug use, recent poly-substance use, recent hard drug use, lifetime hard drug use, problem recognition, and substance use with family were associated with 2MFU hard drug use. Logistic regression results reveal that homelessness (OR=3.1, 95% CI=1.0-9.6, p=.05) and recent hard drug use (OR=2.7, 95% CI=1.1-6.4, p=.02) increased the odds of 2MFU drug use. Recent hard drug users (OR=4.3, 95% CI=1.2-15.4, p=.02) had increased odds of 2MFU hard drug use.
Conclusions: Probation has a limited suppression effect for people with severe substance use disorders. Recent hard drug use predicts future drug use and future hard drug use. The identification of probationers most at risk for failure due to continued substance use should assist probation agencies in targeting probationers for behavioral health services.
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IS HIGH FRUCTOSE CORN SYRUP ADDICTIVE? STUDIES OF OPERANT INTRAORAL SELF-ADMINISTRATION IN RATS.

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Aims: The numerous similarities between obesity and drug dependence suggest that some foods and drugs of abuse may share the ability to reinforce addictive behaviors. The current experiments in male Sprague-Dawley rats employed operant intraoral self-administration and taste reactivity to study and compare the hedonic and reinforcing effects of high fructose corn syrup (HFCS), saccharin and sucrose.
Methods: Animals surgically implanted with intraoral cannulas were tested for orofacial reactions to different sweet solutions and allowed to press a lever to receive infusions of these solutions on continuous ratio (CR) and progressive ratio (PR) schedules of reinforcement.
Results: Experiment 1 (n = 22) revealed that self-administration of HFCS on a CR schedule is sensitive to changes in concentration/infusion (10%, 25% and 50%), and that higher concentrations maintain higher breakpoints (BPs) on the PR schedule. Experiment 2 (n = 22) indicated that intake of HFCS escalates over 3 weeks of self-administration (3 hours a day) because rats develop binge-like patterns of intake. Experiments 2 and 3 (n = 22) clearly indicated that various concentrations of saccharin do not substitute for HFCS, even when hedonic orofacial reactions are equated. Finally, Experiments 4 (n = 20) and 5 (n = 24) revealed that HFCS produces higher hedonic reactions than sucrose, and that at equicaloric concentrations, HFCS is more potent than sucrose (lowers responding on the CR schedule, and supports higher BPs on the PR schedule).
Conclusions: These data in rats suggest that HFCS has unique hedonic and reinforcing characteristics that may cause addictive-like consumption of foods/drinks that contain it.
Financial Support: Studies supported by the Natural Sciences and Engineering Research Council of Canada (NSERC).

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IMMUNIZATION INCREASES THE REINFORCEMENT THRESHOLD BUT NOT ELASTICITY OF DEMAND FOR NICOTINE IN AN ANIMAL MODEL OF NICOTINE REDUCTION POLICY.

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Aims: Reducing the nicotine content in tobacco products is being considered by the FDA as an industry-wide policy to reduce the addictiveness of tobacco products. Medications could enhance the impact of such policy by helping smokers quit or significantly reduce their smoking at higher cigarette nicotine concentrations. By reducing or slowing nicotine distribution to brain, immunotherapy (vaccines or monoclonal antibodies) could increase the reinforcement threshold or elasticity of demand for nicotine, thereby raising the nicotine dose needed to maintain smoking. The purpose of the present study was to examine this issue in an animal model of nicotine reduction policy.
Methods: Rats were trained to self-administer nicotine (0.06 mg/kg) during daily 2 hr sessions. After NSA stabilized, the unit dose was reduced weekly until extinction levels of responding were achieved. Eight rats received weekly infusions of the nicotine-specific monoclonal antibody Nic311 during the dose reduction phase, while eight rats in a control group received infusions of control antibody. Exponential demand-curve analysis was conducted to compare the sensitivity of immunized and control rats to increases in the unit price (FR/unit dose) of nicotine (i.e. elasticity of demand).
Results: Compared to controls, the dose response curve was shifted to the right and the threshold reinforcing nicotine dose was significantly higher in immunized rats (3.1 vs 11.7 μg/kg, $p<0.05$). Although intensity of demand (intake at zero price, Q0) was greater in immunized rats (2.5 vs 1.1 mg/kg, $p<0.01$), there was no difference in elasticity of demand (α).
Conclusions: These findings show that immunization can attenuate the reinforcing effects of nicotine and might compliment nicotine reduction policy by increasing the reinforcement threshold for nicotine.
Financial Support: NIDA R01-DA026444 (LeSage, PI)

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EXAMINING HCV AND OTHER RISKS AMONG RURAL WOMEN OFFENDERS.

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Aims: Drug users are at heightened risk for Hepatitis C (HCV), which is intensified among the increasing number women offenders. The prevalence of drug use and risky behavior among women offenders is also higher than males. This study adds to the limited information on rural women offenders by examining demographic risk factors for HCV among drug using rural women in jail
Methods: After random selection, women in 3 rural jails consented to participate and were compensated for their time. For this analysis 117 rural women were interviewed face-to-face in a private county jail room using computer assisted personal interviews. HCV antibody status was determined using the OraQuick® HCV test. Using Stata 12 SE, multivariate logistic regression determined independent correlates of HCV status.
Results: Participants were white (98%) and 31 years old with no race or age differences by HCV status. Compared to HCV- (n=55), HCV+ n=62) women reported significantly ($p<.05$) more days in the past 6 months use of marijuana (75.0 vs. 38.9 days), heroin (13.7 vs. 2.3 days), Oxycontin (10.6 vs. .84 days), Anti-anxiety meds (90.2 vs. 59.2 days), Meth (42.6 vs. 18.9 days) and Oxycodone (100.2 vs. 61.4 days). HCV+ were also more likely ($p<.05$) to exchange sex for drugs/money (33.9% vs. 14.6%), use drugs before sex (74.2% vs. 51.8%); inject (83.9% vs. 46.4%), inject more drugs in the past 6 months (2.1% vs. .78%) and more likely to be bi-sexual (32.3% vs. 16.1%). Results from the multivariable model using significant variables at the bi-bivariate level revealed the odds of being HCV+ were 4.9 times higher for women who used drugs before sex, and each additional drug injected in the past 6 months increased odds of being HCV+ by almost 4 times.
Conclusions: Findings suggest that HCV positive drug using women in rural jails are more drug involved and at greater risk for injecting and risky sexual behavior. Implications for interventions, community re-entry and treatment will be discussed.
Financial Support: This study is funded by NIDA RO1DA033866,T32DA035200.

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HIV STIGMA AMONG SUBSTANCE-ABUSING PLWH: IMPLICATIONS FOR HIV TREATMENT, ARV ADHERENCE AND DIVERSION.

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Aims: HIV related stigma has a major impact on quality of life and health outcomes among people living with HIV (PLWH); higher levels of HIV-related stigma are associated with lower antiretroviral (ARV) adherence and uptake of medical care, making it difficult for PLWH to receive the benefits of treatment. This paper examines the impact of HIV stigma on care access and ARV adherence and diversion among substance abusing PLWH.
Methods: Using targeted sampling we recruited 503, substance abusing, PLWH in South Florida to complete a single computer assisted interview assessing demographics, substance use/dependence, and mental health. Stigma was measured with the HIV Internalized Stigma Measure which has 4 subscales: stereotypes about HIV, self-acceptance, disclosure concerns, and social relationships.
Results: Those reporting severe substance dependence (55.3%) endorsed higher mean HIV stigma on stereotypes (8.2 vs. 7.3, p=.00), disclosure (4.2 vs. 3.6 p=.00), and social relationships (5.6 vs. 4.6, p=.02) and lower stigma on self acceptance (7.5 vs. 7.8, p=.00). Nearly 50% of the sample reported recent ARV diversion; diverters endorsed significantly higher stigma on disclosure (4.1 vs. 3.7, p=.04). 54.1% of the sample reported 95% ARV adherence; these individuals reported significantly lower stigma on disclosure (3.7 vs. 4.1 p=.05) and social relationships (4.9 vs. 5.4 p=.04). Those reporting access to HIV care had significantly lower stigma on disclosure (3.8 vs. 4.6, p=.02) and social relationships (5.0 vs. 6.4, p=.00).
Conclusions: Higher levels of HIV stigma are associated with substance dependence, mental health issues, and ARV diversion; lower levels of stigma are associated with better adherence and access to HIV treatment. Our findings have critical public health implications, including the importance of intervention development to decrease HIV related stigma among vulnerable populations.
Financial Support: This research was supported by Grant Number R01DA023157 from the National Institute on Drug Abuse.

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MIXED AMPHETAMINE SALTS-EXTENDED RELEASE FOR ADHD ADULTS WITH COCAINE USE DISORDER.

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Aims: Methylphenidate has produced modest effects in treating ADHD in those with substance use disorders, and the impact of treating ADHD on reducing substance use remains unclear. To date, there have been no controlled published studies evaluating amphetamine analogues. The purpose of this 13 week double-blind, placebo-controlled, two-site trial was to evaluate the efficacy of two robust doses of mixed amphetamine salts-extended release (MAS-ER; Adderall-XR®) as a treatment for ADHD and cocaine dependence.
Methods: 126 ADHD adults with CUD were randomized to an active medication dose (60 or 80 mg of MAS-ER a day) or placebo. Participants had to meet DSM-IV criteria for adult ADHD and cocaine dependence. Participants were titrated up to 60 mg/day or 80 mg/day of MAS-ER and maintained on this dose for 11 weeks. All patients received weekly individual cognitive behavioral therapy.
Results: The randomized sample was predominantly male (84%) and 57% Caucasian, with 75% of the sample being retained through the maintenance phase (week 13), with no group differences. The primary ADHD outcome measure, >/= 30% reduction in ADHD symptoms from last week in trial to baseline, was significantly different across the 3 groups (p=.0046) with the greatest difference between the 60 mg and placebo groups (p=.0018). Notably, covarying for baseline cocaine use, the proportion of cocaine positive weeks over the study's duration was significantly different across the 3 study groups ($p = .005$) with the 80 mg MAS-ER producing significant less cocaine positive weeks than the placebo arm (p=.0009) and the 60 mg arm (p=.08). There were 2 serious adverse events, neither was deemed medication related.
Conclusions: This is the first pharmacotherapy trial evaluating an amphetamine analog for adults with ADHD and CUD. These preliminary data suggest that high dose MAS-ER is well-tolerated and is superior to placebo in reducing both ADHD symptoms and cocaine use.
Financial Support: Supported by NIDA Grants: RO1 023652 and K02 00465

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PREDICTORS OF RETENTION IN METHADONE MAINTENANCE TREATMENT DIFFER BY GENDER.

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Aims: Retention in methadone maintenance treatment (MMT) for at least one year has been associated with positive outcomes. Predictors of retention in MMT have traditionally collapsed across gender. This study hypothesizes that predictors of retention will differ between men and women, and aims to determine which factors best predict retention for each gender.
Methods: Data were collected from the files of 290 patients (173 M, 117 F) admitted to MMT at an outpatient clinic in Detroit between 2002 and 2007. The modal participant was a 50-year old African American (84.8%) male (59.7%).
Results: Although 35.3% of men and 44.4% of women remained in treatment for over a year, gender did not significantly predict treatment retention (χ^2 (1)=2.47, p=.12). In the overall sample, Kendall correlations (dfs=282) revealed that presenting a urine sample positive for opiates, cocaine, or THC metabolites (rs= .29, .29, .24, respectively, all ps < .001) during the first month of treatment, having a DSM-IV diagnosis of cocaine dependence (r = .24, p <.001), a non-drug Axis I diagnosis (r = .12, p = .05), or a history of emotional abuse (r = .12, p = .05) was associated with retention of less than one year. Stepwise logistic regression computed for each gender with years of opioid use entered in step 1 and the variables above entered in step 2 indicated that for males, significant predictors of retention for less than a year were: presenting a urine sample that was positive for opioids (OR=6.6) or THC metabolites (OR=4.9), having a diagnosis of cocaine dependence (OR=2.7), or a non-drug Axis I diagnosis (OR=2.1). For females, significant predictors were: presenting a urine sample positive for cocaine (OR=3.6) or THC metabolites (OR=4.9), and having a history of emotional abuse (OR=2.4).
Conclusions: These findings indicate that predictors of retention in MMT differ between males and females. Future studies on MMT outcomes should consider the unique pathways by which females and males adhere to, and benefit from, MMT.
Financial Support: Joe Young, Sr./Helene Lycacki Funds (State of Michigan)

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STRESS-RELATED GENES AND HEROIN ADDICTION: A ROLE FOR FUNCTIONAL *FKBP5* VARIANTS.

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Aims: To determine if specific single-nucleotide polymorphisms (SNPs) in stress-related genes are associated with heroin addiction.
Methods: Case-control hypothesis-driven association study of 112 SNPs from 26 stress-related genes.
The sample consists of 852 case subjects and 238 controls. The case subjects are former heroin addicts with a history of at least 1 year of daily multiple uses of heroin, treated at a MMTP. European ancestry was verified by ancestry informative markers (AIMs). Association analysis was performed by logistic regression.
Results: Nineteen SNPs in 9 genes (*AVP*, *CRHR1*, *CRHR2*, *FKBP5*, *NR3C2*, *AVPR1A*, *GAL*, *GLRA1* and *NPY1R*) showed nominally significant association (p<0.05) with heroin addiction. Two tightly linked *FKBP5* SNPs, rs1360780 and rs3800373, from intron 2 and the 3' UTR, respectively, remained significant after correction for multiple testing (experiment-wise p =3.0E-04; OR = 2.35; 95% CI,1.5-3.7 & p = 1.6E-05; OR = 2.85; 95% CI,1.8-4.6, respectively).
Conclusions: The study provides evidence for the association of *FKBP5* SNPs with heroin addiction. These SNPs were previously associated with diverse affective disorders and showed functional differences in gene expression and stress response. The *FKBP5* gene encodes a co-chaperone that regulates glucocorticoid sensitivity. The modulation of the stress response by FKBP5 may contribute to the development of opiate dependence and in turn FKBP5 may also mediate the abuse potential of opioids. The study also corroborates our and others previous reports of association of *GAL* SNP rs694066 and *AVPR1A* SNPs rs11174811, rs1587097 and rs10784339 with specific general drug addictions and suggests several new associations.
Financial Support: The Adelson Medical Research Foundation and The Shanxi Scholarship Council of China.

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EFFECT OF CO-ADMINISTRATION OF NALOXONE ON INTRAVENOUS HYDROMORPHONE ABUSE POTENTIAL IN NON-TREATMENT-SEEKING, OPIOID-DEPENDENT DRUG USERS.

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Aims: The non-medical use and abuse of hydromorphone (HMO) has increased in the last several years. A modified-release HMO/naloxone (HMO:NAL) combination formulation of opioid agonist and antagonist under development is expected to deter abuse/misuse. The purpose of this study was to evaluate the IV abuse potential of HMO:NAL combinations compared with HMO alone, in non-treatment-seeking, opioid-dependent drug users.
Methods: This was a double-blind, randomized, crossover dose-ratio ranging study. Subjects underwent 1-2 days of dose selection to identify an individualized IV HMO dose (based on self-reported drug use and pharmacodynamic [PD]/safety data). All subjects underwent one day of HMO dose stabilization. In the main study, subjects received 5 single IV doses of HMO with increasing dose ratios of NAL and 1 dose of HMO+NAL placebo. A rescue protocol was implemented in case of withdrawal. Subjective and objective PD measures were assessed at timepoints up to 8 hours postdose, including Drug-Liking visual analog scale (VAS) and assessments of opioid withdrawal (OOWS and SOWS).
Results: Twelve subjects (92% male, mean age 35 yrs) were randomized into the study and received at least one dose of study drug. HMO alone produced subjective effects typical of opioid administration. While HMO:NAL ratios were associated with significant increases in SOWS and OOWS scores (P<0.05). Certain HMO:NAL ratios showed significantly lower effects on most PD endpoints, including Drug Liking VAS (P<0.05), compared to HMO alone.
Conclusions: In this population the IV co-administration of naloxone with HMO had its intended effect of reducing abuse-related opioid effects and inducing withdrawal symptoms; thereby potentially deterring abuse in opioid-dependent subjects. Such a product may have important public health benefits by reducing high-risk IV abuse of prescription opioids intended for oral administration, while continuing to provide pain relief.
Financial Support: Study was funded by Purdue Pharma (Canada).

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CHARACTERIZING SEX DIFFERENCES AMONG PAIN MEDICATION ABUSERS.

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Aims: Sex differences in usage rates, trajectories and consequences have been examined for numerous substances of abuse (e.g., alcohol, cocaine). However, despite increasing national attention to misuse of pain medications (PM), related sex differences remain understudied in treatment populations. To address this issue, we examined inpatients seeking treatment for substance use disorders. Of particular interest were PM usage patterns, usage milestones (i.e., initiation, regular use, problem use), and rates of milestone progression. A contrast group of Narcotic (Narc; e.g., heroin, morphine) users were similarly examined.
Methods: Subjects (N=597) included men (n=283) and women (n=314) endorsing regular use of at least one substance of abuse (ignoring alcohol and nicotine). Ss provided demographic information, substance use histories, and completed measures of negative affect.
Results: Relative to men, women reported higher rates of regular PM use (24.4% of men vs. 37.9% of women), and problem PM use (19.8% vs. 31.5%). No sex differences were noted for Narc use. Based on problem use and self-reported substance preferences, two subgroups were examined in subsequent analyses: PM users (n=85; 26 men), and Narc users (n=49; 23 men). PM women progressed more rapidly than did PM men from regular to problem use (Ms = 3.7 vs. 0.4 yrs). These sex differences were not observed within the Narc group. Furthermore, in the Narc group, men (M=0.6 yrs) and women (M=0.6 yrs) reported progression patterns similar to PM women.
Conclusions: The current study examined PM and Narc use among treatment-seeking individuals. Women reported greater use of PMs and appeared to transition between these stages more rapidly. Although further examination is required, results suggest that women may be particularly susceptible to issues associated with PM misuse. This interpretation is highlighted by the finding that while men appeared to transition from regular to problem PM use over the course of approximately four years, women made this transition in less than half a year, in a manner similar manner to narcotic users.
Financial Support: R01DA13677 (PI: SJN).

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THE USE OF FINGERNAIL DRUG SCREENING IN MULTIPLY CONVICTED OWI OFFENDERS IN KENOSHA COUNTY, WI.

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Aims: Kenosha County has been piloting the use of direct alcohol biomarkers (DBS Phosphatidylethanol and fingernail Ethyl Glucuronide) as part of its evaluation process for multiply convicted OWI offenders. In addition to the alcohol biomarkers, each subject on initial evaluation also had a five drug panel fingernail drug analysis performed to identify those individuals that had a history of binge use of one or more of these common classes of drugs of abuse.
Methods: Kenosha County, beginning in 2011as part of a pilot program, all three or more conviction offenders received as part of their initial evaluation a DBS PEth, a fingernail EtG and a five panel fingernail analysis. Specimens were collected by the subjects themselves under the direct observation of the evaluator. Laboratory testing utilized the proposed SAMHSA hair and nails screening and confirmation cutoffs as proposed in the Federal Register/ Vol. 69, No. 71 / Tuesday, April 13, 2004 / Notices.
Results: 267 subjects met the criteria of three or more OWI convictions. While most agreed to undergo alcohol biomarker testing (235/267 submitted DBS PEth samples with 115 positives (48.9%) and 206/267 submitted fingernail EtG with 110 positives (53.4%)), only 114 of 267 subjects completed a 5 drug panel on fingernails (# of positives: Amphetamine, 2; Opiate, 14; Cocaine, 16; THCCOOH, 15; PCP, Zero).
Conclusions: Since none of the subjects had been convicted of operating while intoxicated with anything other than alcohol, this survey gave us an insight into the potential drug use that this particular population uses. We had no empirical evidence to hypothesize as to the extent of the illicit and Rx drug use that this population might be using at the time of their arrival at evaluation. None self reported a history of other drug use.
We believe that this study under reports the actual drug use since the panel was limited to only a 5-drug panel. A more extended panel including more opioids may have unmasked more use and would be advised for future studies.
Financial Support: Part of the testing was funded through NIAAA 1R43AA016463-02

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THE TRACE-AMINE-ASSOCIATED RECEPTOR 1 AGONIST RO5263397 ATTENUATES ABUSE-RELATED EFFECTS OF COCAINE IN RATS.

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Aims: Cocaine abuse remains a health and economic challenge with no effective treatment available. Trace amine associated receptor (TAAR) 1 knockout mice demonstrate altered response to methamphetamine, suggesting the involvement of TAAR 1 in the behavioral effects of methamphetamine. However, given the lack of selective TAAR 1 ligands, little is known of the behavioral consequences of pharmacological manipulation of TAAR 1. This study reported the effects of a TAAR1 agonist RO5263397 on some abuse-related effects of cocaine in rats.
Methods: Cocaine-induced behavioral sensitization, cocaine-induced conditioned place preference and intravenous cocaine self-administration studies were conducted to evaluate the effects of RO5263397 on these behavioral effects of cocaine.
Results: RO5263397 (3.2-10 mg/kg, i.p.) dose-dependently attenuated the development of behavioral sensitization to daily 10 mg/kg cocaine administration. RO5263397 (3.2-10 mg/kg) attenuated the expression of cocaine-induced conditioned place preference. Behavioral economic analyses revealed that RO5263397 (5.6 mg/kg) significantly increased the elasticity of the cocaine (0.75 mg/kg/infusion) demand curve. RO5263397 (3.2-10 mg/kg) also markedly decreased cue- and cocaine-induced reinstatement of cocaine seeking behavior.
Conclusions: These results suggest that RO5263397 attenuates various abuse-related effects of cocaine and that TAAR 1 may represent a novel drug target for the development of novel pharmacotherapy against cocaine abuse.
Financial Support: Supported by R21DA033426

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MORTALITY AMONG PATIENTS ACCESSING PHARMACOLOGICAL TREATMENT FOR OPIOID DEPENDENCE IN CALIFORNIA, 2006-2010.

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Aims: To examine mortality rates, causes of death, and risk and protective factors for mortality among patients accessing pharmacological treatment for opioid dependence.
Methods: Treatment records were linked to the National Death Index on all patients enrolled in publicly-funded pharmacological treatment programs for opioid dependence in California from 2006 to 2010. Causes of death were coded using ICD-10 criteria. Crude mortality rates (CMR) and standardized mortality ratios (SMR) were calculated. Proportional hazards (Cox) regression was used to identify baseline patient risk factors for death.
Results: Among the sample of 20,408 patients, there were 1,031 deaths (5.1%) over the 5-year follow-up period (52508 person years, median observation time 2.6 years), corresponding to a CMR of 19.6 deaths per 1,000 person-years of follow-up. The SMR was 5.5 (95% CI 5.2-5.9), representing a more than five-fold increase of mortality risk. The leading causes of death were related to drug use (43%), cardiovascular disease (14%), and trauma (11%). Hepatitis and HIV-related illness accounted for 4% and 1% of deaths, respectively. Approximately 22% of deaths occurred while the patient was in treatment. Of patients that died out of treatment, 7% of deaths occurred within seven days of treatment discharge. Patient baseline characteristics associated with a higher risk of death included older age, being male, African American race/ethnicity, injection drug use, unemployment, and mental illness. Future analyses will examine how mortality is associated with treatment experiences.
Conclusions: The elevated risk for mortality among patients receiving treatment for opioid dependence underscores the need to develop interventions that reduce the risk of relapse. Future analyses will aim to identify treatment-level risk and protective factors for mortality.
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A NON-PARAMETRIC APPROACH IDENTIFIES A NEW GENE-GENE INTERACTION ASSOCIATED WITH PROGRESSION OF NICOTINE DEPENDENCE.

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Aims: To detect gene-gene interactions pertinent to progression of nicotine dependence (ND) by employing a new survival approach.
Methods: In this work, we propose a non-parametric weighted Nelson-Aalen (WNA) approach. Simulations have been carried out to compare the performance of WNA versus conventional Cox-regression-based approaches (CRB). An empirical study was also conducted by applying WNA to three independent datasets from the Study of Addiction: Genetics and Environment (SAGE).
Results: WNA outperformed CRB in simulations. For the SAGE data analysis, 2 SNPs from genes GRIK2 and CSMD1 were associated with ND progression ($p<0.001$) in the initial dataset (n=1276). The joint association was replicated in two independent datasets (n1=1420; n2=1425). Further inquiry favors potential GRIK2-CSMD1 interaction and importance for ND progression.
Conclusions: Better performance of WNA over CRB approaches can be explained: 1) WNA assumes no patterns of hazard functions, yielding robustness under various disease scenarios; 2) Unlike CRB approaches, WNA's forward selection algorithm selects a model and uses cross-validation to determine model complexity, adding robustness. SNPs associated with GRIK2 and CSMD1 were jointly associated with ND. GRIK2 is associated with smoking cessation, while CSMD1 is highly expressed in the central nervous system. This biologically plausible conclusion requires further replication and confirmation in other empirical studies.
Financial Support: Supported by: NIDA K01DA033346 (QL) & K05DA015799 (JCA).

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EXPANSION OF BUPRENORPHINE OPIOID AGONIST THERAPY IN THE UNITED STATES: FACILITY-LEVEL FACTORS.

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Aims: Buprenorphine opioid agonist therapy (OAT) is an effective treatment for opioid use disorder, and its use has the potential to increase the proportion of patients receiving any OAT. We sought to understand to what extent characteristics of facilities contribute to the broader diffusion of buprenorphine OAT over time.
Methods: We examined data from the NSSATS, which collects information annually from all public/private substance abuse treatment facilities in the US. We determined the proportion of facilities that provide methadone and buprenorphine OAT and the proportion of patients prescribed buprenorphine in each facility, from 2004 to 2011 and described the influence of facility characteristics on buprenorphine OAT provision.
Results: From 2004 to 2011, the percentage of facilities using buprenorphine-OAT increased (2.4% to 11.6%) relative to facilities using methadone (7.4% to 9.2%). The greatest rise in facilities using buprenorphine-OAT occurred within federal facilities (3.7%to 36.8%). The proportion of patients on buprenorphine-OAT within facilities offering buprenorphine-OAT also increased (1.0% to 9.6%). Facilities offering combined mental health/substance abuse services experienced a 452% growth in buprenorphine-OAT. Facility characteristics associated with the greatest proportion of absolute/relative increase in buprenorphine-OAT included general medical services offered, government ownership, large service capacity, and detoxification services offered.
Conclusions: Provision of buprenorphine-OAT has increased over time and was influenced by facility type and characteristics. Further increase in buprenorphine-OAT can occur by increasing the number of programs offering this treatment and increasing the number of patients served within facilities already providing buprenorphine-OAT.
Financial Support: This work was supported by NIDA 1R01DA032881-01A1.

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STRENGTH OF COCAINE-ASSOCIATED MEMORY: ACQUISITION, EXTINCTION AND REINSTATEMENT.

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Aims: Drugs of abuse act as reinforcers because they influence learning and memory. The present study was undertaken to elucidate how varying the stimulus salience of cocaine reward influences a) drug memory strength and b) the mechanisms underlying formation, reconsolidation and extinction of such memories.
Methods: Mice were conditioned by daily fixed doses of cocaine (Fix-C; 11.25 mg/kg) or escalating doses of cocaine (Esc-C; 3, 6, 12, 24 mg/kg) over 4 days. The transition from drug use to drug addiction involves escalation in drug intake. Thus, we posit that administration of escalating doses of cocaine is relevant to the human practice of drug use. We used quantitative polymerase chain reaction (qPCR) and western blot analyses to determine genes and their proteins involved in the development of Fix-C and Esc-C memory. Differences in a) acquisition, b) reconsolidation and c) stress-induced reinstatement between Fix-C and Esc-C were investigated. The forced swimming test (FST) was used as a model for stress-induced reinstatement.
Results: Training by Esc-C resulted in elevated hippocampal levels of Grin2b mRNA and its protein NR2B compared to training by Fix-C. The neuronal nitric oxide synthase (nNOS) inhibitor 7-Nitroindazole (7-NI) a) attenuated acquisition b) disrupted reconsolidation and c) eliminated stress-induced reinstatement of Fix-C but not Esc-C memory. Antagonism of NR2B-containing N-methyl-D-aspartate (NMDA) receptor using ifenprodil a) attenuated acquisition and b) disrupted memory reconsolidation of both Fix-C and Esc-C memory.
Conclusions: Results suggest that varying the stimulus salience of cocaine reward during conditioning engages different neural pathways in the formation of cocaine associated memory. While Fix-C memory is nitric oxide (NO)-dependent, Esc-C memory bypasses the dependence of NO signaling. Further, the NR2B subunit of NMDA receptor plays a key role in the development of cocaine-associated memory following an escalating regimen of cocaine.
Financial Support: Supported by R01DA026878 and R21DA029404

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SUBSTANCE USE AND RISK PROFILES OF ADOLESCENT MEDICAL PATIENTS.

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Aims: Many adolescents with asymptomatic HIV/STI or STI-related symptoms do not seek treatment services and those who do access the health care system may not be screened for HIV. Further, adolescent medicine clinics have low rates of substance use screening and referral. This study examines the risk profiles of patients attending an adolescent health clinic located in a predominately African American and Latino neighborhood and how substance use interacts with sexual risk behavior.
Methods: An electronic intake is completed by every new patient and patient not seen at the clinic in the previous 12 months. Clinic intake data from new and returning patients (N=250) was analyzed. Patients reported lifetime and recent sexual behavior, condom use, pregnancy, STI diagnosis, and substance use.
Results: In the prior 3 months, substance use was high (59% alcohol, 57% marijuana, 34% other substances), as was sexual risk behavior (89% vaginal sex, 25% anal sex, 61% no condom at last intercourse, 20% never use a condom, 21% Chlamydia). Patients who report substance use are more likely to report sexual activity. Patients who report an STI are also more likely to report substance use, with the relationship between marijuana and STI diagnosis being significant (p=0.015). Patients reporting substance use were also less likely to be consistent condom users.
Conclusions: This study suggests that adolescents self-referring to an adolescent health clinic are likely to engage in multiple risk behaviors and involvement in sexual risky behavior is related to substance use. Therefore, there is a significant need for medical providers to screen adolescents for both sexual risk behaviors and substance use, which provides an opportunity for comprehensive care.
Financial Support: NIDA R34DA031806

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CANNABIS SELF-ADMINISTRATION IN THE LABORATORY AND USE IN THE NATURAL ENVIRONMENT DURING OUTPATIENT TIAGABINE MAINTENANCE.

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Aims: The GABA reuptake inhibitor tiagabine produces behavioral and therapeutic effects that overlap with Δ9-THC, and therefore might be useful as a medication for cananbis-use disorders. The purpose of this study is to determine the ability of outpatient maintenance on tiagabine to reduce cannabis self-administration in the laboratory and use in the natural environment.
Methods: Non-treatment-seeking daily cannabis users are maintained on tiagabine (0 and 12 mg/day) on an outpatient basis for two weeks. Subjects receive financial incentives for abstinence, verified by semi-quantitative urinalysis. Medication compliance is managed via Wisepill® technology, which permits real-time monitoring. On the final four days of each maintenance condition, subjects participate in two 2-session blocks (one sampling and one self-administration session) to assess the reinforcing, subjective, performance and physiological effects of smoked cannabis (0 and 5.7% Δ9-THC).
Results: Seven subjects have completed the protocol; additional subjects will be enrolled until the target number have completed. Review of the data collected to date suggests that tiagabine alone and in combination with cannabis has been well tolerated. Subjects have been abstinent 31% of study days, which did not differ by maintenance condition. Cannabis has functioned as a reinforcer, increased positive subjective effects ratings, impaired psychomotor performance and elevated heart rate. Tigabine has had minimal effect on the response to cannabis, although heart rate and a small number of subjective effects questionnaire items appear attenuated during tiagabine maintenance.
Conclusions: The limited impact of tiagabine could be a function of dose, which is lower than the therapeutic range. Future studies will incorporate higher tiagabine doses and larger financial incentives to better model the motivation to quit. Overall, these results demonstrate the feasibility of using outpatient maintenance procedures to screen potential medications for cannabis-use disorders.
Financial Support: Supported by K02 DA031766, R01 DA025605 and UL1TR000117.

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PRESCRIPTION OPIOID MISUSE AMONG YOUTH IN PRIMARY CARE: A COMPARISON OF RISK FACTORS.

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Aims: The rise in prescription opioid misuse (POM) is an emerging public health problem that often begins in adolescent years. Because these substances can originate from prescribers, it is vital to examine this issue in the primary care setting. Among a sample of youth who presented to primary care clinics, we assessed past 3 month misuse of prescription opioids as well as other substance use and obtained an assessment of psychosocial risk factors.
Methods: Data are from a sample of primarily African-American (62.6%) youths ages 12-18, presenting to primary care community health clinics (Federally Qualified Health Centers) in two urban settings in the United States (n=1076) that were enrolled in a prevention and early intervention study. We grouped participants into those reporting baseline opioid misuse (n=79), those who used other substances (n=330) including alcohol, marijuana, and misuse of other prescription drugs, and non-users (n=667).
Results: In comparison to participants who used other substances, those with POM began using marijuana and alcohol at younger ages, had higher likelihood of other prescription drug misuse, and higher likelihood of binge drinking (45.6% vs 24.2 %). Compared to those who used other substances, those who misused opioids also had higher frequency of delinquency, higher levels of psychiatric symptoms with a particularly high percent reporting suicidal thoughts or behaviors (30.4% vs 10.6%). Multinomial regression revealed that among a range of risk factors, youth with POM were significantly less likely to be African-American (OR: 0.36 95% CI: 0.21-0.63), more likely to have non-violent delinquency (OR:1.06 95% CI: 1.01-1.12), and more likely to have suicidal thoughts or attempts (OR: 2.33 95%CI: 1.18-4.59) compared to those who used other substances.
Conclusions: Adolescents with POM have higher rates of other substance use and other psychosocial risk factors compared to those who use other substances. Future studies are needed to better understand what contributes to these differences.
Financial Support: NIDA #DA020075; 2013-2014 NIDA-AACAP Resident Research Award in Substance Abuse and Addiction

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SUSTAINED-RELEASE METHYLPHENIDATE FOR THE TREATMENT OF METHAMPHETAMINE DEPENDENCE.

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Aims: Recent research indicates that methylphenidate (MPH; Concerta®) may be effective in reducing amphetamine/methamphetamine (MA) use in drug-dependent individuals. The aim of this study was to investigate sustained-release methylphenidate (MPH) for reducing MA use in MA-dependent adults.
Methods: 110 participants were randomized to active drug (MPH=55) or placebo (PLB=55) at two sites (Los Angeles, Honolulu) in a 10-week, double-blind, placebo-controlled study. The active phase included daily doses of 18mg for Week 1, 36mg for week 2, and 54mg for weeks 3-10. Daily single-blinded placebo was provided to all participants in weeks 11-14. Twice-weekly clinic visits included medication dispensing, urine toxicology testing (UDS), assessments, and motivational incentives for MA-negative UDS. Once-weekly group Cognitive Behavioral Therapy was provided.
Results: Participant baseline characteristics include a mean age of 39 years, 81.8% male, 60% White, 23.6% African-American, 11.4 mean years of MA use, 12.2 mean days of MA use in the prior 30 days, and 43.6% provided a MA-positive UDS. No difference was found between groups in days of MA use during the last 30 days of the active phase (p=0.22); however, the MPH group had a greater reduction in MA use days from baseline through the active phase (MPH=6.56; PLB=3.82, p=0.05). The MPH group also had lower craving scores and fewer marijuana-positive UDS than the PLB group, but the groups had similar retention, other drug use, adverse events, and treatment satisfaction.
Conclusions: MPH may be an effective treatment for individuals with moderate to severe MA use disorder.
Financial Support: NIDA DA015084; Medication provided by Janssen Pharmaceuticals

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RELATIONSHIP OF TRAIT IMPULSIVITY AND LIFETIME COCAINE USE CONSEQUENCES TO CURRENT DEPRESSION.

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Aims: Determine whether trait impulsivity and lifetime cocaine use consequences (severity, number of consequences) are related to current depressive symptoms. Improve understanding of the psychological mechanisms and outcomes associated with regular cocaine use.
Methods: Regular cocaine users (n = 90) were recruited to participate in assessment and experimental research. Barratt Impulsivity Scale subscales (motor, attentional, non-planning) were used to measure trait impulsivity; Beck Depression Inventory (BDI-II) was used to measure past 14-day depressive severity. We assessed cocaine dependence severity by interview (Cocaine Selective Severity Assessment [CSSA]) and number of lifetime cocaine use consequences by questionnaire (Drug History Use Questionnaire [DHUQ]).
Results: Higher motor, attentional, and non-planning impulsivity scores were associated with earlier age of first cocaine use and higher degree of current depression. Non-planning impulsivity was positively related to both increased cocaine-related severity (CSSA) and a greater number of lifetime cocaine use consequences (DHUQ). Higher cocaine-related severity scores and more lifetime cocaine use consequences were associated with higher depression severity scores. Higher non-planning impulsivity was related to increased cocaine use severity and consequences. In multiple-mediation tests, cocaine use severity partially mediated (r2 = .42) the relationship between non-planning impulsivity and current depression. Also, the number of lifetime cocaine use consequences partially mediated the relationship between impulsivity and current depression (r2 = .32).
Conclusions: These results highlight trait impulsivity as a risk factor for cocaine-related adverse consequences. These findings also demonstrate that cocaine-related consequences may function in a more nuanced manner than just an outcome of impulsivity, but as a pathway between trait impulsivity and current depression.
Financial Support: NIH R01 DA026861 and Joe Young Sr./Helene Lycacki Funds (State of Michigan).

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MEASUREMENT OF ATTENTIONAL BIAS AND STRESS IN CHRONIC MARIJUANA USERS.

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Aims: For nearly 40 years marijuana has remained the most widely used illicit drug in the US, accounting for about 60% of illicit substance use disorders (SUD) in the US. More than 50% of first-time users are under age 18. There is compelling evidence that the phenomenon of cue reactivity is related to drug seeking and relapse. Attentional bias (AB) is a measurable component of cue reactivity, and can be operationally defined as differential attention (e.g., reaction time difference) towards drug-related stimuli vs. neutral stimuli. This phenomenon has been demonstrated in SUD populations across many classes of abused drugs, including MJ. Cue reactivity and AB are exacerbated by acute and chronic stress and anxiety. Notably, stress is a well-documented predictor of MJ abuse and relapse.
Methods: We developed a novel target detection task that capitalizes on the salience of pictorial stimuli (marijuana-related and neutral pictures) and short cue-probe onset timing in order to maximize AB effects, and utilized this task to measure interactions between AB to MJ cues and stress in 13 subjects with MJ SUD and 13 age-matched control subjects.
Results: As measured by reaction time differential following MJ vs. neutral cues, we found a statistically significant group x stress interaction. Follow-up tests revealed that MJ SUD subjects with high stress levels displayed significantly greater AB to MJ cues when cue presentations were short (125 ms) but not long (250 ms). AB was not observed under any condition in the control group. Additionally, on the signal detection measure criterion C, we observed a significant group x cue type interaction. MJ SUD subjects showed a bias to respond 'yes' to targets in the presence of MJ cues and "no" to neutral cues, while control subjects showed the opposite pattern.
Conclusions: The novel cue-probe task may prove useful as laboratory index of cue reactivity and relapse risk in MJ SUD. Additionally, the task may be sensitive to trait measures and manipulations of stress and anxiety.
Financial Support: NIH / NIDA P50 DA 09263; R21 DA 034825

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GROWTH MODELS OF MATERNAL PERINATAL DRINKING PATTERNS IN A NATIONAL SAMPLE.

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Aims: Childbirth and early parenting represent an important transition in a woman's life characterized by psychosocial, economic and logistic changes. Substance use during this critical period of time poses significant risks for women and child's health. Alcohol is among one of the most used substances. The harmful effects of alcohol use during pregnancy have been widely documented elsewhere. Importantly, as high as one in five women report alcohol use during pregnancy and a significant proportion of those who quit during pregnancy return to drinking post-delivery. The purpose of this study is to understand the longitudinal pattern of maternal drinking before, during and after pregnancy and the role of maternal characteristics. This study succeeds the limitations of past studies that did not examine the longitudinal trend of maternal perinatal alcohol use with a sufficiently long follow up period.
Methods: Latent growth models were used to describe the average pattern of maternal drinking frequency at six time points, from preconception through child entry to kindergarten (N=9,100 mothers from the Early Childhood Longitudinal Study (ECLS-B) representing the 2001 U.S. birth cohort).
Results: Results revealed a significantly decreasing trend in maternal alcohol use over this time period. Significantly different patterns of drinking were revealed for different profiles of maternal characteristics and behavior measured at baseline. For example, better educated mothers and those who smoke exhibit higher level drinking preconception and mothers with postpartum depression decreases drinking at a slower pace.
Conclusions: Findings highlight the importance of understanding the developmental patterns and risk factors of maternal alcohol use during the critical time period of perianal and early parenting. Study results inform the design and implementation of new prevention strategies for women and child's health.
Financial Support: The research was funded by the National Institute on Drug Abuse (grant 1 R01 DA 030496-01A1, Social Ecology of Maternal Substance Use, to principal investigator Dr. Elizabeth A. Mumford).

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PROCEDURE-DEPENDENT EFFECTS OF ANTAGONISM OF NICOTINIC ACETYLCHOLINE RECEPTORS ON CONDITIONED NICOTINE SEEKING IN RAT MODELS OF SMOKING RELAPSE.

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Aims: Our previous studies have demonstrated a role of nicotinic acetylcholine receptors (nAChRs), specifically the α7 subtype, in conditioned incentive properties of nicotine cues. The present study examined effects of pharmacological antagonism of the two major nAChR subtypes, α4β2 and α7 nAChRs, on cued nicotine seeking with an emphasis on the comparison between an abstinence-alone and an extinction-reinstatement procedures.
Methods: Male Sprague-Dawley rats were trained in daily 1-h sessions to intravenously self-administer nicotine (0.03 mg/kg/infusion, free base) on a fixed ratio 5 schedule. A nicotine-conditioned cue was established via association of a sensory stimulus (5-s tone/20-s lever light on) with each nicotine infusion. In the abstinence-alone procedure, rats remained in their home cages for two weeks, whereas in the extinction-reinstatement procedure, lever responding was extinguished in ten daily sessions over a two-week period. Then, lever responses with contingent re-presentations of the nicotine cue without availability of nicotine were examined after pretreatment with antagonists at the nAChRs.
Results: In the abstinence-alone rats, neither dihydro-β-erythroidine (DHβE, α4β2-selective antagonist) nor methyllycaconitine (MLA, α7-selective antagonist) altered the cue-maintained lever responses. In the extinction rats, however, MLA but not DHβE significantly suppressed the cue-reinstated lever responses.
Conclusions: These results demonstrated the conditioned incentive properties of nicotine cues independent of testing procedures. Interestingly, the sensitivity of cued nicotine seeking to pharmacological blockade of nAChRs, the α7 but not α4β2 subtype, was observed in the extinction-reinstatement but not the abstinence-alone procedure. The findings suggest that neurobiological changes involving α7 nAChRs may have accrued during the extinction of nicotine-reinforced responding. Further examination of the procedural differences between abstinence-alone and extinction is warranted.
Financial Support: NIH/NIDA grant R01DA17288 and funds from the University of Mississippi Medical Center.

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PROFILING ALCOHOLIC DRINKING AND DATING PSYCHOLOGICAL ABUSE IN A SAMPLE OF COLLEGE STUDENTS IN CHINA.

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Aims: China has experienced dramatic growth in alcohol consumption with the largest production of alcohol beverage in the world at present. The purpose of this research is to explore preliminary data to assess dating psychological abuse among a sample of college students in Eastern China.
Methods: Upon the university IRB approval, an online survey was self administered by a group of 3rd and 4th year medical students in two coastal cities in Eastern China. As part of an ongoing study starting Oct 2013, 76 of 110 students completed the survey at a response rate of 69%. Questions on drinking, smoking, exposure to Western culture, as well as a questionnaire of Dating Psychological Abuse and Victimization were asked.
Results: Participants were aged between 19 - 24 years, about equal proportion were male and female. No significant difference was found in parental education. About 70% of participants reported ever use of alcoholic beverage in their lifetime: 26% reported every drunk or binge drinking (risky drinkers) and the remaining 43% reported drinking without any episode of being drunk or binge drinking (light drinkers). More risky drinkers were male ($p<0.05$). Comparing to light drinkers, more non-drinkers and risky drinkers reported experiencing dating psychological abuse than light drinkers ($p<0.05$) and spent less time on media in English (including TV, Internet, radio, newspaper or magazine or smart phone) as a measure of exposure to Western culture ($p<0.05$).
Conclusions: Even though Chinese student risky drinking behaviors are not as common as in the U.S., non-drinkers and risky drinkers were more likely to experience dating psychological abuse than light drinkers. Potential risk factors or mechanisms for such abuse need to be further explored in non-drinkers and risky drinkers.
Financial Support: None

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EFFECTS OF EXTENDED RELEASE TRAMADOL ON CIGARETTE SMOKING DURING OPIOID WITHDRAWAL.

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Aims: ER tramadol has a metabolite (M1) with modest opioid agonist activity and is under investigation as a treatment for opioid withdrawal. Opioid agonists have been shown to increase cigarette (cig) smoking. The aim was to evaluate the effects of ER tramadol on cig smoking during opioid withdrawal.
Methods: This is a secondary analysis from an inpatient, double blind, randomized, placebo-controlled trial. Eligibility criteria included: 18-55 years old, short-acting prescription opioid use > 20 of the last 30 days, meeting DSM-IV criteria for current opioid dependence, and daily cig smoking. The day after admission, subjects were randomly assigned to oral placebo or ER tramadol (200 or 600 mg daily) for 7 days and allowed to smoke their preferred brand of cigs ad lib. Breakthrough withdrawal medications were available for all subjects. Outcomes collected daily were: 1) subject and nursing report of number of cigs smoked, 2) number and weight of smoked cig butts, and 3) the brief questionnaire of smoking urges (QSU). Fagerstrom Test for Nicotine Dependence (FTND) score and maximum total doses of withdrawal medications/day (proxy for opioid withdrawal severity) were employed as covariates.
Results: Subjects (n=11-12/group) smoked a mean of 21.1 cigs/day prior to admission. No group smoked more than this during admission. Cig butts showed a Group x Time [$F(2.080)$; $p=0.02$] interaction whereby the 600 mg group had more butts collected than the placebo group on days 1-3. There were no other significant Group effects in time course or peak maximum value analyses. FTND was a significant covariate ($p<0.05$) for number of cigs smoked and butts collected and peak QSU Factor 1 (smoking for positive reinforcement) score.
Conclusions: ER tramadol has few effects on smoking during opioid withdrawal. Limitations include inpatient setting and lack of positive opioid agonist control condition.
Financial Support: NIDA R01 DA027068 (MRL), T32 DA007304 and NCRR and NCATS UL1RR033173.

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RELATIONS BETWEEN PSYCHOPATHY FACTORS, SUBSTANCE USE DISORDERS, AND TREATMENT READINESS AMONG ADULTS IN INPATIENT SUBSTANCE USE TREATMENT.

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Aims: Psychopathy refers to a maladaptive personality profile comprised of interpersonal/affective (Factor 1 traits and Coldheartedness) and behavioral characteristics (Factor 2 traits). Research supports a relationship between psychopathy and substance use, but individual factors are not often examined. In the present study, we hypothesized that interpersonal and affective traits would be related to less treatment motivation while behavioral traits would be related to more dependence and drug-related problems among adults in residential treatment.
Methods: Participants were 81 adults in residential substance use treatment. At treatment entry, using the SCID-IV, participants were interviewed regarding cocaine, heroin, marijuana, and alcohol use in the past year, as well as symptoms of substance dependence. Self-report measures included measures of psychopathy, readiness/motivation for treatment, and a measure of drinking/drug related problems.
Results: We examined the relationships between psychopathy factors (Factor 1/Fearless Dominance, Factor 2/ Impulsive Antisociality, and Factor 3/ Coldheartedness) and drug use related outcomes. Factor 1 traits were inversely associated with cocaine use ($r = -.35$, $p < .01$) and dependence ($r = -.25$, $p < .05$), motivation/readiness for treatment ($r = -.28$, $p < .05$), and problems associated with use ($r = -.26$, $p < .05$). In contrast, Factor 2 traits were positively associated with marijuana use ($r = .37$, $p < .01$) and problems associated with use ($r = .37$, $p < .01$). Coldheartedness was positively associated with marijuana dependence ($r = .26$, $p < .05$) but negatively related to self-reported drinking/drug use problems ($r = -.31$, $p < .01$).
Conclusions: Generally, interpersonal and affective features of psychopathy (Factor 1 traits and Coldheartedness) were negatively related to use, dependence, drug-related problems, and treatment readiness. In contrast, the behavioral features of psychopathy (Factor 2 traits) were positively related to these outcomes.
Financial Support: NIDA R01 DA19405; NIDA T32 DA028855

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AVAILABILITY OF WOMEN-CENTERED DRUG TREATMENT SERVICES: AN ANALYSIS OF NSSATS 2002-2010.

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Aims: The importance of gender in drug treatment has been well described in research and it is now generally accepted that women who receive gender specific treatment services have better outcomes than those who do not. However little is known about how this has translated into treatment service development. This study will use the National Survey of Substance Abuse Treatment Services (NSSATS) to investigate the availability of women centered treatment options throughout the US over time.
Methods: NSSATS 2002-2010 an annual survey of treatment facilities receiving federal funding was used. Facilities with specific programs for women were contrasted with those that without. The availability of additional services of benefit to women and families (such as child care, trauma-related counseling and special programs for pregnant/postpartum women) were investigated. Services were compared over time and by geographic variation using STATA v 11.
Results: Over 13,000 participated in the survey each year with a slight decline over time of the proportion reporting specific programs for women (38% in 2002 vs 32% in 2010, $p<0.001$). There was a slight increase in facilities providing transportation (35- 38%) and domestic violence counseling (33-36%), minimal change in child care (9-8%) and a decline in pregnant/postpartum services. Facilities that reported specific programs for women were more likely to also report trauma-related counseling, child care, housing assistance and domestic violence counseling ($p<0.001$ for all). There was a decline in women centered services across a geographic gradient from 41% in urban areas to 20% in small non-urban adjacent regions ($p<0.001$).
Conclusions: There has been minimal change in women centered services in drug treatment facilities over time. Marked geographic disparities exist for all components of women centered care.
Financial Support: None

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NEUROPSYCHOLOGICAL CHANGES DURING RESIDENTIAL SUBSTANCE USE TREATMENT.

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Aims: To examine whether neuropsychological functioning improves as a result of substance use treatment from baseline to 30-day follow-up among clients at an inpatient alcohol and drug treatment facility.
Methods: Participants (N=322; M age=39; 76% male) were recruited from a 30-day inpatient treatment facility. Participants completed WebNeuro twice as part of standard care, once following detoxification and again at discharge. WebNeuro, an online neuropsychological assessment, takes 45 minutes to complete. WebNeuro is comprised of several subtests (e.g., finger tapping test, digit span) that load onto four cognitive domains: Thinking based on attention, memory and overall executive functioning; Emotion comprised of emotional facial identification and recognition and reaction biases; Self-Regulation assessing emotional resilience, social skills and positivity bias; and Feeling based on anxiety, depression and stress scores.
Results: Gender, age, and education were found to be significantly correlated with the four domains and were controlled for in the analyses. Preliminary analyses revealed that mean Thinking ($F(1,322)=7.85$, $p=.005$) and Feeling ($F(1,322)=18.60$, $p=.000$) domains significantly differed between time points whereas Self-Regulation trended toward significance ($F(1,322)=3.30$, $p=.07$) and Emotion did not ($F(1,322)=.675$, $p=.41$). Increased scores across domains at inpatient treatment completion indicate improvements in neuropsychological functioning that might be attributable to treatment.
Conclusions: Findings demonstrated that neuropsychological functioning improved in patients during a 30 day residential substance use treatment program. This research helps target specific areas of neuropsychological functioning affected by substance use and the degree to which abstinence can positively impact restoration in the domains of Thinking and Feeling. Future research should continue to focus on how these improvements vary based on drug of choice and length of use.
Financial Support: No financial support was received for the present study.

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EFFECTS OF SMOKING CESSATION ON POSTPARTUM DEPRESSION.

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Aims: Smoking is a risk factor for postpartum depression; women who smoke during pregnancy report more depressive symptoms, including clinically-significant levels, compared to nonsmokers or those who quit. While correlational studies have confirmed robust associations between smoking & risk for postpartum depression, whether smoking cessation decreases depression risk has not been established. The purpose of this study was to use data from controlled clinical trials on voucher-based incentives for smoking cessation to examine if smoking cessation directly decreases depressive symptoms in recently postpartum women.
Methods: Participants (N=289) were smokers at the start of prenatal care. Women were randomly assigned to receive vouchers contingent on biochemically-verified smoking abstinence (n=167) or a control condition were vouchers were given independent of smoking status (n=122). Incentives were available from study entry until 12wks postpartum, with a follow-up at 24wks. BDI scores & smoking status were assessed at all assessments. Chi-squares & ANOVAs were used to compare dichotomous & continuous variables, respectively.
Results: Incentives increased abstinence above control levels antepartum & postpartum: (late-pregnancy: 37% vs 11%; 2wk: 33% vs 15%; 4wk: 31% vs 12%; 8wk: 25% vs 10%; 12wk: 22% vs 7%; 24wk: 15% vs 3%; all $p < .001$). Average BDI scores among contingent women were significantly lower than controls from weeks 2-12 postpartum (2wk: $p < .05$; 4wk: $p < .005$; 8wk: $p < .01$; 12wk: $p < .05$). Incentives also significantly reduced the proportion of women with BDI scores in the clinical range (i.e., BDI > 16) at weeks 4-12 postpartum, all $p < .05$).
Conclusions: In addition to increasing smoking abstinence, voucher-based incentives for smoking cessation decrease postpartum depression. This effect compliments the significant improvements in birth outcomes & breastfeeding duration reported previously with this intervention.
Financial Support: R01DA14028, R01HD075669, P20GM103644, T32DA07242

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PATHWAYS TO CHANGE: TRAJECTORIES FOLLOWING TREATMENT IN WOMEN WITH CO-OCCURRING PTSD AND SUBSTANCE USE DISORDERS.

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Aims: High rates of relapse, heterogeneity, and nonlinearity in substance/alcohol use following treatment have underscored the need for clinical research to examine longitudinal trajectories of growth or decline. The present study evaluated the trajectories of substance/alcohol use in the 12 months following treatment in a sample of 353 women with co-occurring substance use disorders (SUDs) and posttraumatic stress disorder (PTSD). A second, related aim was the exploration of associations between common trajectories and risk factors, treatment response, and post-treatment behaviors.
Methods: Study re-analyzed data from the largest randomized, multi-site clinical trial to date for co-occurring SUDs and PTSD in women (National Institute on Drug Abuse Clinical Trials Network "Women and Trauma Study"). We utilized latent growth mixture models (LGMM) with multiple groups to estimate substance and alcohol use trajectories of 353 women with comorbid PTSD and SUDs who received six session of either Seeking Safety or Women's Health Education in addition to substance abuse treatment. LGMM was then employed to identify variables significantly associated with membership in each trajectory class.
Results: LGMM analyses indicated the best fit model to consist of three distinct use patterns in the year following treatment: 1.) a "light use" group (54.5%) with low likelihood and low frequency of use 2.) a "lapsing" group (23.6%) with high likelihood and low frequency 3.) a "relapsing" group (21.9%) with high likelihood and high frequency. PTSD treatment response, age, and follow up care were associated with specific trajectories.
Conclusions: Study marks the first application of LGMM to investigate post-treatment substance/alcohol use trajectories in women with co-occurring PTSD and SUDs. Findings supported a 3-class trajectory model. Findings highlight the necessity of accounting for heterogeneity in post-treatment substance/alcohol use and the relevance of incorporating methodologies like LGMM when evaluating treatment outcomes.
Financial Support: NIDA: U10 DA13035 (Edward Nunes, PI).

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ORBITOFRONTAL CONNECTIVITY IN MARIJUANA SMOKING YOUTHS WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

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Aims: Overlap in behavioral, neuropsychological and neurobiological deficits have been observed between ADHD and marijuana (MJ) users suggesting that understanding the neurobiological deficits associated with core symptoms of ADHD may lead to new insights into the development of MJ use disorders. Orbitofrontal (OFC) circuits have been implicated in both adolescent MJ use and ADHD, therefore the current study evaluated OFC functional connectivity between 3 groups of youths: healthy controls (HC), heavy MJ using youths, and youths with MJ and comorbid ADHD (MJ+ADHD).
Methods: Functional MRI resting-state data was obtained on 31 HC, 43 MJ and 14 MJ+ADHD participants. Factorial analyses controlling for both age and gender were performed for the three groups with group as an effect for the left and right OFC separately.
Results: Differences in OFC functional connectivity were observed in youths with MJ only and MJ+ADHD as compared to HC in frontal and motor regions. In addition, differences between the MJ and MJ+ADHD groups were also found between right OFC and the left frontal lobe. Furthermore, both MJ and MJ+ADHD had increased functional connectivity in the right OFC with age of first MJ use, suggesting that aberrant connectivity of the right OFC may be a shared predisposing factor for substance use initiation in both groups. In contrast, lifetime MJ use was associated with increased OFC functional connectivity to posterior brain regions in MJ only youth whereas increased OFC functional connectivity to frontal regions was evident in MJ+ADHD youth.
Conclusions: These findings indicate both overlapping and unique patterns of connectivity among young MJ smokers with and without ADHD. The findings of atypical OFC functional connectivity patterns in youths with MJ use only and MJ+ADHD may be related to the suboptimal decision making capacities and increased impulsivity leading to substance use initiation, abuse and dependence evident in both populations.
Financial Support: K23 MH087831, 1R01 DA020269

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EFFECTS OF IMMIGRATION TO THE UNITED STATES ON ALCOHOL, TOBACCO AND CANNABIS USE AMONG COLOMBIAN ADOLESCENTS.

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Aims: Increased exposure to the US culture has been consistently linked to increased substance use among Latino adolescents. This project aims to explore differences in the lifetime and past year use of alcohol, tobacco and cannabis among Colombian adolescents in Colombia and Colombian adolescents in the US and to examine whether length of residence in the US has an effect on the use of these substances.
Methods: Data from the US R-DAS National Surveys on Drug Use and Health for 2002-2009 were analyzed and compared with data from the Colombian 2004 National School Survey on Psychoactive Substance Use. The US survey was designed to yield nationally representative probability samples of 12-17 year olds and the Colombian survey was designed to yield a nationally representative sample of school adolescents. Estimates of alcohol, tobacco and cannabis use were obtained for Colombians residing in the US with different length of residence. Prevalence estimation involved weights and Taylor series linearization approaches for variance estimation.
Results: Compared to Colombian adolescents living in the US, Colombian adolescents in Colombia exhibit higher lifetime (74.9% vs. 53.4%) and past year (61.9% vs. 45.4%) prevalence of alcohol use, higher lifetime (46.1% vs. 27.9%) and past year (30.6% vs. 16.0%) prevalence of tobacco use, and similar lifetime (7.6% vs. 9.4%) and past year (6.7% vs. 6.6%) prevalence of cannabis use. Length of residence in the US did not affect significantly lifetime prevalence estimates of any of the substances under study.
Conclusions: In contrast with previous research these cross-national comparisons suggest that adoption of US cultural values could be beneficial for Colombian immigrant adolescents, particularly in regards to diminishing alcohol and tobacco use. Selective migration as well as the observed increase in use of these substances among Colombian adolescents in Colombia over the last decade could help to explain the findings.
Financial Support: Supported by: MDLR (MD002288); CLQ (DA026401 & MD002288)

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UNDERSTANDING ORGANIZATION READINESS TO USE OF TECHNOLOGY-BASED TREATMENT APPROACHES.

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Aims: The potential for technology to meet growing demand for substance use and mental health care is strong. Little is known about readiness of substance abuse and mental health treatment organizations to implement technology-based treatment, and barriers to use of technology approaches are not well understood. Online survey methodology was used to examine individual and organizational characteristics associated with readiness to use technology-based tools and to identify primary barriers to use of technology for behavioral health care.
Methods: Survey was distributed to the membership network (N=1900) of the National Council for Behavioral Health. Target respondents were care decision-makers, including administrators, supervisors, program directors and providers. The survey tapped individual and organization demographics as well as organizational readiness to change and climate, technology readiness and current technology use. One open-ended item assessed perceptions of barriers to use of technology-based therapeutic tools.
Results: Of 431 valid respondents, 260 completed the open-ended question. Respondents were primarily non-Hispanic white and representative of broad age and experience ranges. Sample was geographically diverse, representing 43 states and the District of Columbia. Readiness for technology use was high. Current use of technology in care was low. Technology readiness was associated with organizational motivation to change and climates marked by openness to innovation. Implementation barriers included: Cost, Privacy Concerns, Lack of Awareness about technology approaches, Infrastructure limitations, Perceived Negative Impact, Access, Provider Openness, Support, and Reimbursement.
Conclusions: Results are discussed in light of the need for training about the potential for technology-based therapeutic tools to enhance behavioral health care. Solutions for implementation barriers will be outlined and directions for research and policy initiatives will be described.
Financial Support: This study was supported by funding from 1P30DA029926-01.

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HEIGHTENED VULNERABILITY ASSOCIATED WITH CRIMINAL JUSTICE INVOLVEMENT AMONG WOMEN WHO USE DRUGS.

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Aims: To assess whether criminal justice (CJ) involvement is associated with increased socioeconomic vulnerability among women who use drugs.
Methods: People who had smoked crack and/or injected drugs in the past 6 months were recruited using targeted sampling methods in Oakland, CA from 2011 to 2013. Participants (N=2171) received rapid HIV testing and counseling and participated in a quantitative interview. For this analysis, we examined female participants only (n=856). We defined CJ involvement as arrest, incarceration or community supervision (probation or parole).
Results: CJ involvement was very high among women who use drugs in this community-based sample. Ninety percent of women reported lifetime CJ involvement and 30% reported CJ involvement in the 6 months prior to interview. Compared to women without CJ involvement in the past 6 months, recently CJ-involved women were more likely to be homeless (60% vs. 38%, p<.01), to trade sex for drugs (34% vs. 22%, p<.01), to have injected drugs (33% vs. 18%, p<.01) and to have experienced physical violence (38% vs. 22%, p<.01) in the past 6 months. Drug treatment utilization was slightly more common among CJ-involved women (19% vs. 13%, p=.05). In addition, HIV testing in the past 6 months was more common among CJ-involved women (30% vs. 16%, p.<.01), although few of these women were tested in CJ settings.
Conclusions: Women with recent CJ involvement were substantially more vulnerable to homelessness, violence and risky forms of drug use than their non-CJ-involved counterparts. Their participation in drug treatment and HIV testing was somewhat higher, although drug treatment utilization was quite low overall. Encounters with the CJ system should be used as opportunities to link women to stabilizing social services, such as drug treatment and housing.
Financial Support: NIMH grant #R01MH094090; NIMHD grant #R01MD007679

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IMPLEMENTING OPIOID OVERDOSE EDUCATION AND NALOXONE DISTRIBUTION IN AN OUTPATIENT COMMUNITY TREATMENT PROGRAM.

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Aims: In an attempt to address a significant local increase in mortality from opioid overdose, we are beginning a series of interventions used to blend an abstinence-based outpatient treatment program with overdose prevention interventions including naloxone. The education component is meant to be a culturally competent intervention that can be effectively implemented in a suburban outpatient treatment program. By addressing the knowledge-based and moral concerns of patients and their social support systems, education is expected to facilitate the distribution of naloxone as a life-saving treatment.
Methods: A multi-phasic approach is being used to provide opioid dependent patients in a suburban outpatient treatment program with access to education and medication that have been shown effective in other populations. Patients are first educated on naloxone as a life-saving intervention and how to obtain the medication from providers or distribution sites within their communities. Later, concerns of the patients' social supports will be addressed by formally educating families and significant others on relapse rates of opioid dependent patients, as well as the efficacy of naloxone. Next, overdose education will be combined with on-site training on use of naloxone and ultimately with direct distribution of naloxone kits to patients and families during the treatment program.
Conclusions: Providing opioid overdose education and naloxone distribution within an abstinence-based community treatment program may raise concerns about supporting continued substance use, but appropriate education can mitigate these concerns and increase access to a potentially life-saving treatment.
Financial Support: Linden Oaks Hospital at Edward

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MOTIVES UNDERLYING THE ASSOCIATION OF BORDERLINE PERSONALITY DISORDER AND ALCOHOL-RELATED PROBLEMS.

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Aims: BPD is characterized by emotion dysregulation, unstable relationships, and high rates of engagement in risk behaviors, including substance abuse. It is estimated that 58% of people with BPD report a lifetime diagnosis of AUDs and people with BPD experience a disproportionate burden of substance-related problems. Little research has explored motivational factors that underlie the relationship between BPD and alcohol-related consequences. Theories of BPD suggest that risk behaviors may serve both affect regulatory and interpersonal functions, but these perspectives have not been tested directly. The aim of this study was to examine the relationship between BPD and alcohol-related consequences, while exploring coping and conformity motives for alcohol use as possible mediators of this relationship.
Methods: Sixty-nine young adults (n = 28 with BPD) participated as part of a larger study, where they completed a semi-structured interview to diagnose BPD and other clinical disorders, followed by self-report measures of motives for alcohol use (DMQ) and alcohol-related consequences (BYAACQ). Path analysis was used to examine coping and conformity motives as mediators of the relationship between BPD and alcohol-related consequences.
Results: Results revealed that BPD was significantly and positively associated with alcohol-related consequences, B = 2.43, p = .04. The indirect effect of BPD on alcohol consequences was significant through both coping motives, B = 1.30, p < .05 and conformity motives, B = .96, p < .05. When the proposed mediators were included in the model, the direct effect of BPD on alcohol consequences was no longer significant, p = .86, indicating full mediation.
Conclusions: Results support coping and conformity motives as mediators of the relationship between BPD and alcohol-related consequences. Individuals with BPD may experience higher levels of alcohol-related consequences because they use alcohol as means to manage negative affect and avoid interpersonal rejection.
Financial Support: UMD Dept. of Psychology

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TO REDUCE OR ABSTAIN? SUBSTANCE USE GOALS IN THE TREATMENT OF VETERANS WITH SUBSTANCE USE DISORDERS AND COMORBID PTSD.

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Aims: Posttraumatic stress disorder (PTSD) and substance use disorders (SUDs) frequently co-occur, and recent developments have been made with integrated treatments. Previous SUD research demonstrates the importance of goal choices, however, we are not aware of any studies to date that have examined goal choices in the context of SUD/PTSD treatment. To address this gap, we investigated correlates of reduced use vs. abstinence goal choices among treatment-seeking Veterans with SUDs and PTSD. We hypothesized that a reduced use goal would be associated with less severe SUD symptoms.
Methods: Participants (N=45) completed the Addiction Severity Index-Lite, MINI International Neuropsychiatry Inventory, Clinician Administered PTSD Scale, Beck Depression Inventory, substance use goal assessment.
Results: Approximately half (55.6%) chose a goal to reduce use of substances. Participants who chose to reduce, as compared to abstain, evidenced less severe alcohol dependence (p = .04), less chronicity of use (p = .09), fewer prior contacts with alcohol/drug (p = .05) or other mental health treatment (p = .04), higher employment functioning (p = .01), and more severe PTSD symptoms (p = .05). Logistic regression yielded a model in which alcohol dependence severity (OR = 0.212, 95% CI = .051–.885, p = .03) and employment functioning were the only significant predictors of goal choice (OR = 0.354, 95% CI = .130–.963, p = .04).
Conclusions: The findings replicate clinically relevant differences among participants who chose to abstain vs. reduce substance use. Also, the present study demonstrated that higher PTSD symptom severity was related to a reduction goal. It may be that abstinence is perceived as less attainable in the face of higher PTSD severity, particularly if substance use has been a means of self-medication. Future research should investigate the effects of treatment goals on SUD and PTSD treatment outcomes, and the nature of changes in treatment goals across time.
Financial Support: R01 DA030143 (Back, SE)

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SEX, DRUGS AND HEALTHCARE UTILIZATION AMONG HIV+ PATIENTS: THE ROLE OF MARIJUANA.

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Aims: People living with HIV/AIDS (PLWHA) are among the heaviest users of medical marijuana (MJ), but little is known about effects of MJ on mental health, pain and other health problems, acute care utilization, and other substance use in PLWHA. This study assessed the impact of MJ use on health outcomes, health care utilization, and risk-transmission behaviors in PLWHA.
Methods: Patients attending an urban HIV clinic completed self-report surveys and underwent clinician interviews to provide data on MJ and other drug use, physical and mental health symptoms, health care utilization, and risky sexual behaviors.
Results: The present analysis compared 3 groups of patients (total N=98) who differed in marijuana use: 28 reported no MJ use (non-users), 32 reported regular use but did not meet DSM-IV Dependence criteria (non-dependent), and 38 met these criteria (dependent). Compared to both MJ user groups, non-users were older but did not differ in years since HIV diagnosis or years spent at the HIV clinic, and reported fewer past 3-month ER and urgent clinic visits. Non-users also reported fewer and less severe GI, neurological, cognitive, respiratory, and mood complaints. Nonusers were older at initiation of alcohol use, reported less lifetime and recent alcohol use, and fewer reported use of cocaine and opioid painkillers compared to the MJ users. The two MJ user groups did not differ on any health outcomes, age at first MJ use, years of regular use, frequency of use, and grams smoked/day. In all cases, regular MJ use predated HIV diagnosis. Non-users were less likely to report engaging in risky sexual behaviors over the past month, including having fewer sexual partners, less frequent anal sex, and more frequent use of condoms.
Conclusions: MJ use is common in these HIV+ patients, and is associated with more health complaints and healthcare utilization. Regular non-dependent users did not differ from dependent users, indicating that cannabis dependence is not necessary for poorer health outcomes in this at-risk population.
Financial Support: NIH R01 DA032678 and Joe Young, Sr./Helene Lycaki Funds (Michigan)

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WITHDRAWN

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MODELING POTENTIAL MECHANISMS OF DIFFERENTIAL TREATMENT EFFECTS IN OSMOTIC-RELEASE METHYLPHENIDATE FOR SMOKING CESSATION.

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Aims: Existing data suggest that osmotic-release methylphenidate (OROS-MPH) is superior to placebo for smoking cessation in patients with higher baseline attention deficit hyperactivity disorder (ADHD) symptom severity, but inferior to placebo for those with lower baseline symptom severity. The causal mechanism for this differential treatment effect is unclear.
Methods: We dissected the possible casual mechanisms behind this differential treatment effect using a moderated mediation analysis using data from a 14-week, multi-center, randomized trial with 255 patients. We modeled prolonged abstinence and ADHD severity at the end of the trial as a function of evolving craving and withdrawal symptoms measured through the trial follow-up period.
Results: For patients with lower baseline ADHD symptom severity, OROS-MPH treatment is associated with an improvement of withdrawal symptoms, but not of craving. For patients with higher baseline ADHD severity, OROS-MPH is significantly associated with improvement of both craving and withdrawal symptoms. The OROS-MPH related improvement of craving occurs a few weeks after the initiation of nicotine replacement in patients with high baseline ADHD severity.
Conclusions: The positive effect of OROS-MPH in patients with higher baseline ADHD symptom severity may be partially mediated through its preferential effect on nicotine craving in this group. The negative effect of OROS-MPH in patients with lower baseline ADHD symptom severity is not mediated by any of the analyzed intermediate outcomes.
Financial Support: NIDA-CTN grants U10 DA013035 (Dr. Nunes) and U10 DA013732 (Drs. Winhusen and Somoza) and by NIDA grants K24 DA022412 (Dr. Nunes) and K24 DA029647 (Dr. Levin), as well as a grant from the Leon Levy Foundation (Dr. Luo).

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MOOD, ALEXITHYMIA, DISPOSITIONAL MINDFULNESS, SENSITIVITY TO REWARD AND PUNISHMENT, FRONTAL SYSTEMS FUNCTIONING AND IMPULSIVITY IN CLIENTS UNDERGOING TREATMENT FOR SUBSTANCE USE DISORDERS.

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Aims: Mood and presumed sub-cortical and frontal lobe related traits were assessed in 100 in-patients undergoing treatment for substance use disorders and in a community control sample of 107 social drinkers.
Methods: Participants completed self-report measures of mood, alexithymia, dispositional mindfulness, frontal systems functioning, impulsivity, sensitivity to rewards and punishments, alcohol use, illicit drug use and demographic characteristics.
Results: Multivariate analysis of covariance (MANCOVA) controlling for age, education, previous serious head injury and gender revealed highly significant differences ($p < .0001$) between clinical and control groups on all dependent measures. The clinical group scored significantly higher on depression, anxiety, stress, alexithymia, frontal systems dysfunction, reward sensitivity, punishment sensitivity and impulsivity, and lower on dispositional mindfulness, than the control group. Time in treatment was significantly correlated only with levels of depression, anxiety and stress, supporting the relative stability of the trait measures.
Conclusions: Results are consistent with the notion that substance use disorders are linked to frontal lobe dysfunction and associated traits, although the current findings cannot determine whether such characteristics predated or post-dated disordered substance use.
Financial Support: This research was funded by a Bond University Vice-Chancellor's Research Grant.

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COCAINE USE-RELATED TEMPORAL CHANGES IN WHITE MATTER AS DETECTED BY DTI.

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Aims: Diffusion tensor imaging (DTI) has been used to study cocaine use disorder (CUD) compared to controls. Results of several studies showed that CUD patients (CUDs) have lower fractional anisotropy (FA) in several brain regions, including the corpus callosum (CC), suggesting compromised white matter in CUDs. However, few studies have examined DTI longitudinally in CUDs and non-drug using controls (NCs) to assess whether FA changes over time in CUDs.
Methods: DTI images were acquired from 11 CUDs (9 males) and 11 NCs (9 males). Each subject was scanned twice. The 2nd scan was conducted 69.7±16.3 days after the 1st scan. All the DTI images were processed using the FSL software FDT and TBSS. Changes in FA over time were examined in whole brain using FSL Randomise, separately in CUDs and NCs.
Results: There was no significant difference (t=0.85, p=0.20) in age between CUDs (42.8±6.3 yrs) and NCs (38.7±8.0 yrs). CUDs showed active cocaine use prior to the 1st scan with at least 1 positive UDS for cocaine during screening. CUDs were then enrolled in a treatment study. 10 of the 11 CUDs continued cocaine use during treatment as shown by a positive UDS for cocaine prior to the 2nd scan. NCs had negative UDS for drugs of abuse at the time of both scans. There was no significant change in whole brain FA between the 2 scans for NCs. However, CUDs showed significantly ($p<0.05$, 2-tail) reduced FA in body, splenium of CC, and several other white matter regions.
Conclusions: The DTI findings in the CC are consistent with previous studies showing CUD is associated with reduced FA in the CC. The temporal changes in FA observed in CUDs who continued to use cocaine but not in CNs suggest that cocaine use over a 10 week time frame could lead to changes in white matter as measured by DTI, and that DTI could be a potentially sensitive/useful biomarker for the treatment of CUD.
Financial Support: Funded by NIDA Grants # R01 DA034131 (LM) / P50 DA009262 (FGM/JLS).

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CORRELATES OF DRUG USE PROBLEMS AMONG SUBSTANCE USERS PRESENTING IN EMERGENCY DEPARTMENTS: RESULTS OF A MULTI-SITE STUDY.

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Aims: Drug-related emergency department (ED) visits have steadily risen over the years, with substance users relying heavily on the ED for medical care. The present study aims to identify clinical correlates of problematic drug use that would facilitate identification of ED patients in need of substance use treatment.
Methods: Using previously validated tests, 15224 adult ED patients across 6 academic institutions were pre-screened for drug use as part of a large randomized prospective trial. Data for 3240 participants who reported using their primary drug of use in the past 30 days were included. Self-reported variables related to patient demographics, substance use, and ED visit were examined to determine their correlative value for problematic drug use.
Results: Of the 3240 patients, 2084 (64.3%) met criteria for problematic use (Drug Abuse Screening Test score ≥3). Age >30, tobacco smoking, daily or binge alcohol drinking, daily drug use, primary non-cannabis drug use, resource-intense ED triage level, and perceived drug-relatedness of ED visit were highly correlated with problematic drug use. Among primary cannabis users, correlates of problematic drug use were similar with the exception of age, with younger adults more likely to have problematic use, and ED triage level, which had no correlative value.
Conclusions: Clinical correlates of drug use problems may assist the identification of ED patients who would benefit from intervention. While cannabis users report problems with their drug use the least, there are some indicators useful in identifying those for whom cannabis use may be causing problems. The correlation between problematic drug use and resource-intense ED triage levels suggests that ED-based efforts to reduce the unmet need for substance use treatment among a population less likely to access primary care may help decrease overall health care costs.
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PLANNED DISINHIBITION? RISKY SEXUAL BEHAVIOR, PROBLEMATIC ALCOHOL USE, AND GENDER.

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Aims: Recent research has highlighted a positive association between heavy drinking and prevalence of risky sexual behavior. Consistent with these results, the current study hypothesizes problematic drinking will be positively associated with high-risk sexual behaviors in a young adult population.
Methods: College students (49% male) with an average age of 18.8 (1.4) were recruited to participate in a study investigating risk behavior. Presented here is preliminary data (n = 63) investigating links between self-reported drinking behavior from the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) and sexual behavior from the sexual risk survey (SRS; Turchik & Garske, 2009). The SRS inquires about the number of occasions for specific sexual behaviors in the past 6 months. In addition to a total score, the SRS has five subfactors: sexual risk taking with uncommitted partners, risky sexual acts, impulsive sexual behaviors, intent to engage in risky sexual behaviors, and risky anal sex acts.
Results: Preliminary results indicate that total AUDIT was a significant predictor of the total SRS score ($p < .001$). Follow-up regression analysis demonstrated the AUDIT is a significant predictor of sexual risk taking with uncommitted partners ($p < .001$), impulsive sexual behaviors ($p < .001$), and intent to engage in risky sexual behaviors ($p < .001$). Predictions with risky sexual acts and risky anal sexual acts were not significant (p's > .1). Additionally, gender moderated the relationship between impulsive sexual behaviors ($p < .01$) and intent to engage in sexual behaviors ($p < .01$). Higher problematic drinking is associated with increased number of sexual behaviors and intent to engage in sexual in males compared to females.
Conclusions: Preliminary analyses support the hypothesis that sexual risk taking is associated with problematic drinking; however, factors associated with risky sexual acts, such as unprotected sex, were not significantly associated with problematic drinking. Instead, increased problematic drinking is associated with increased sex partners in both genders, but increased sexual behaviors and intent in males.
Financial Support: None

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CHOICE SELF-ADMINISTRATION IN THE HIV-1 TRANSGENIC RATS: A PERSPECTIVE ON COMPULSIVE BEHAVIOR.

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Aims: One main criterion for diagnosing drug addiction is the reduction or cessation of nondrug activities in favor of drug seeking and compulsive drug consumption (APA, 2000). Utilizing a choice self-administration (CSA), the volitional response of selecting drug over a highly-palatable sucrose alternative was studied in the HIV-1 transgenic (HIV-1 Tg) rat.
Methods: Adult female, ovariectomized, HIV-1 Tg (n=14) and control (CTRL-F344; n=15;) rats were used. All animals had prior experience responding for sucrose with FR (5% w/v) and PR (1 – 30% w/v) schedules of reinforcement, and subsequent experience responding for cocaine with FR (0.33 mg/kg/inj), and PR (0.01 – 1.0 mg/kg/inj) schedules of reinforcement. The CSA sessions required earning 2 nondrug and 2 drug rewards before initiation of the choice component.
Results: Despite the history of cocaine self-administration, volitional responding in the first session indicated a clear preference (~2.5X) for sucrose over drug. However across 5 choice sessions, relative drug taking increased and sucrose taking decreased ($F(1,6)=30.3$, $p \leq 0.002$). Responding during a drug extinction session displayed a clear preference for sucrose (~1.7X over saline). This overall choice profile was driven by the volitional responding of the F344 control animals ($F(1,6)=38.5$, $p \leq 0.001$). In contrast, the HIV-1 Tg rats displayed a more consistent preference (~2.9X) for sucrose over drug across the 5 choice sessions ($F(1,7)=5.8$, $p \leq 0.05$).
Conclusions: Self-administration trained rats, with a history of both sucrose and cocaine rewards, initially abstained from a return to drug use in favor of sucrose reward. With continued opportunity, a very clear shift to cocaine taking, and away from the nondrug sucrose option, was noted. This changing profile was consistent with a compulsive drug consumption perspective and reflected the prominent profile displayed in the F344 control rats. Chronic expression of the HIV-1 transgene, however, disrupted this choice profile.
Financial Support: NIH grants R01DA013137, R01HD043680, R01DA021287, T32GM081740.

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THC (Δ9-TETRAHYDROCANNABINOL) ELICITS PERSISTENT CHANGES IN EXPRESSION OF GENES IMPLICATED IN ADOLESCENT NEURODEVELOPMENT.

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Aims: Compared with adult-onset initiation, the adolescent is more susceptible to the adverse consequences of marijuana, including higher prevalence of addiction, altered brain morphology, reduced IQ, and psychosis. We hypothesized that THC alters adolescent brain development by modifying expression of genes implicated in dopamine signaling, guiding adolescent mesocortical dopamine development and vascular endothelial growth.
Methods: We treated adolescent rats (PND 28) with THC (10 rats; 1.5 mg/kg i.p., every 3rd day) or vehicle (10 rats). Ten subjects were euthanized 24 hr after the last injection (PND 50), and 10 were euthanized 2 weeks later in early adulthood (PND 64). Gene expression levels were measured in cerebellum, frontal cortex, hippocampus, and striatum, using real-time PCR. The average fold change values with standard errors were analyzed for statistical significance, using a two-tailed, paired t-test.
Results: . THC altered expression of genes implicated in neurodevelopment, dopamine circuitry, vascular endothelial growth and dopamine signaling, with the most significant changes two weeks after drug cessation, during transition from adolescence to adulthood. For certain genes, expression profile changes were similar in different brain regions. DCC, a guidance molecule essential for mesocortical dopamine circuitry during adolescence, was consistently altered in 3 of 4 brain regions. Dopamine signaling genes (receptors, transporter) were up-regulated by THC.
Conclusions: These findings suggest that THC affects genes critical for dopamine signaling, neurodevelopment, vascularization, and guidance of mesocortical dopamine circuitry during the transition from adolescence to adulthood. The findings have implications for the reported anatomical and/or functional abnormalities detected in brain regions of early initiators of marijuana use.
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EFFECT OF OPIOID WITHDRAWAL ON DELAY DISCOUNTING OF FOOD IN RHESUS MONKEYS.

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Aims: Opioid abusers discount the value of delayed reinforcers more rapidly than non-users; however, it is unclear how chronic drug use or its discontinuation (i.e. withdrawal) impacts discounting. This study examined the effects of chronic morphine treatment and discontinuation of treatment on delay discounting of food in rhesus monkeys (n=3).
Methods: Responding on one lever delivered 1 food pellet immediately and responding on another lever delivered 2 food pellets either immediately or after a delay (30, 60, or 120 sec) that increased across blocks within the session. First, the acute effects of morphine (0.032-5.6 mg/kg) on choice were determined, after which monkeys received morphine daily for at least 3 weeks followed by 1 week during which treatment was discontinued. During each subsequent period of morphine treatment and discontinuation, the treatment dose increased up to a dose of 3.2 mg/kg twice daily.
Results: Monkeys responded predominantly for the large reinforcer when both reinforcers were delivered immediately and progressively more for the smaller, immediately available reinforcer as the delay to the large reinforcer increased. When administered acutely, morphine had variable effects on choice across monkeys but consistently, and dose-dependently, decreased response rate. Tolerance to the rate-decreasing effects of morphine was progressively greater as the treatment dose of morphine increased, and physical dependence emerged as indicated by marked decreases in response rate upon discontinuation of daily morphine treatment. Discontinuation of treatment did not appear to systematically impact discounting; that is, delay functions were not consistently shifted in one direction. However, choice patterns were more variable across sessions following discontinuation of treatment as compared to during treatment.
Conclusions: Increased variability in choice potentially reflects degradation in the control of reinforcer delay and might contribute to continued drug use.
Financial Support: Supported by NIH Grants R01DA029254, K05DA017918 (CPF), T32DA031115 (DRM), and F32DA035605 (DRM).

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ASSESSING STANDARDS OF EVIDENCE IN EVIDENCE-BASED PROGRAM REGISTERS FOR BEHAVIORAL HEALTH TREATMENTS.

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Aims: There has been a proliferation of "what works" types of program registers on the internet, intended to assist policy-makers and practitioners in identifying "evidence-based" treatments and practices. The study's aim was to identify and describe the characteristics of such evidence-based program registries (EBPRs) in behavioral health treatment (i.e., related to drug/alcohol addiction and/or mental disorders).
Methods: The study conducted a comprehensive search of the internet to identify EBPRs that included behavioral health-related treatments and interventions. Each register was classified on two dozen variables with particular emphasis on the type and strength of evidence of effectiveness required by the registers in rating programs and modalities.
Results: 18 relevant EBPRs were identified; 11 rate the effectiveness of individual treatment programs (e.g., National Registry of Evidence-Based Program and Practices); 3 rate only modalities of treatment; and 4 consist of systematic reviews/meta-analyses (e.g., Cochrane and Campbell Libraries). Among the 14 EBPRs rating individual programs or modalities, 4 consider only the results of randomized controlled trials (RCTs), another 4 also consider certain quasi-experimental designs, and 6 place no restrictions on acceptable designs. For programs to qualify as evidence-based, 3 registries require a minimum treatment effect size which is statistically significant; 2 require a significant effect, but no minimum effect size; 7 require some indication of effect, but not necessarily significant; and 6 have no specific requirement. Concerning risk of bias in studies, there is considerable variability among registers in what components are considered: implementation fidelity (78%), attrition (67%) and validity of measures (61%), statistical power (50%), excluded items (39%), allocation concealment (22%), blinding (17%),
Conclusions: Different EBPRs use very different standards of evidence in rating the effectiveness of behavioral treatment programs. This can be confusing to policy-makers and practitioners.
Financial Support: Supported by NIDA grant R21DA032151

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OPIOID SUBSTITUTION TREATMENT PROTECTS AGAINST HEPATITIS C VIRUS ACQUISITION IN PEOPLE WHO INJECT DRUGS: THE HITS-C STUDY.

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Aims: While evidence of the effectiveness of opioid substitution treatment (OST) in reducing HIV transmission among people who inject drugs (PWID) is strong, less is known about its impact on hepatitis c virus (HCV) transmission. Despite increasing evidence of the protective effects of OST in combination with other interventions, a recent systematic review concluded there was insufficient evidence of the effectiveness of OST alone in preventing HCV infection in PWID. We aimed to estimate HCV incidence and identify associated risk and protective factors among PWID in Sydney, Australia.
Methods: HCV antibody negative PWID (n=156) were enrolled in a prospective observational study – the Hepatitis C Incidence and Transmission Study – community (HITS-c). Interviewer-administered behavioural questionnaires and serological assessments were conducted every 24 weeks. Incidence was estimated using the person-time method.
Results: Incidence of HCV was 7.9/100py, substantially lower than the 44.1/100py observed a decade previously in a similar cohort in urban Sydney. Younger age (AHR 5.10; 95% CI 1.54-16.81, p=0.007), daily or more frequent injecting (AHR 3.91; 95% CI 1.13-13.49, p= 0.031) and not being on OST for those who mainly injected heroin (AHR 4.42; 95% CI 1.02-19.20, p< 0.047) were independently associated with incident infection.
Conclusions: Incidence of HCV among PWID in Sydney has declined substantially over the last decade. Ours is the first community-based prospective observational study to observe an independent protective effect of OST against HCV infection. This is likely due to increased coverage of OST and needle and syringe programs combined with a decrease in the population of PWID.
Financial Support: This study was initially funded by the University of New South Wales Hepatitis C Vaccine Initiative and subsequently by the National Health and Medical Research Council (Project Grant #630483).

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WITHDRAWN

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COGNITIVE AND CARDIOVASCULAR EFFECTS OF CARVEDILOL IN RECENTLY ABSTINENT, COCAINE-DEPENDENT PATIENTS.

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Aims: Determine if there were differences between placebo (PLA) vs. carvedilol (CRV) (50mg/day) in terms of withdrawal symptoms, cognitive functioning, and psychosocial assessments during the two week residential stay in this 12-wk, double blind, placebo-controlled clinical trial.
Methods: COC dependent participants were placed in research beds at a residential treatment facility then randomized by sex, race and drug withdrawal severity, to receive either carvedilol (N=13) or placebo (N=14). Participants participate in the Substance Abuse Day Treatment Program (wks 1-2). Withdrawal, craving, side effects and sleep assessments were obtained three times weekly, while mood and cognitive assessments were obtained weekly.
Results: Med groups differed on subject characteristics with PLA subjects more likely to be male (92.9% v 53.8%, p=0.03), employed (92.9% v 46.2%, p=0.03) and have a lifetime alcohol use disorder (16.8+/-14.7 vs.8.2+/-11.0 weeks, p=0.05). There was a significant sex effect for alcohol craving (p=.03), performance on Stroop (p=.05), Trails B (p=.02) and Digit Symbol substitution (p=.001) tests. There were no clinically significant differences between medication groups or over time for blood pressure or heart rate.
Conclusions: These very preliminary results suggest that carvedilol seems to be well tolerated from a cardiovascular risk standpoint. Sex-driven differences appear to be the cause of the results obtained thus far.
Financial Support: Supported by NIDA grants DA018197-06, T32DA022981

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FEASIBILITY OF VERY LOW DOSE NALTREXONE AND BUPRENORPHINE TRANSITION FROM OPIOID USE TO EXTENDED-RELEASE NALTREXONE.

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Aims: The approval of extended release injectable naltrexone suspension (XR-NTX) has introduced a new option for treating opioid addiction, but the absence of physiological opioid dependence is a necessary and challenging first step for starting therapy. Outpatient detoxification gives poor results and inpatient detoxification is either unavailable or too brief for the physiological effects of opioids to resolve. We summarize findings from an open label study that tested whether the transition from opioid addiction to XR-NTX can be safely and effectively performed in an office-based setting using very low dose oral naltrexone and buprenorphine/naloxone (NTX/BUP).
Methods: Twenty-four treatment seeking opioid addicted individuals were given increasing doses of naltrexone starting at 0.25 mg with decreasing doses of buprenorphine starting at 4 mg during a 7-day outpatient XR-NTX induction procedure. Withdrawal discomfort, craving, drug use, and adverse events were assessed daily until the XR-NTX injection, then weekly over the next month.
Results: Seventeen of the 24 participants received XR-NTX and 16 completed weekly assessments. Withdrawal, craving, and opioid or other drug use were significantly lower during induction and after XR-NTX administration compared with baseline (range: t/ $\chi 2$ = 4.8-7,8, p = 0.002-0.0001), and no serious adverse events were recorded.
Conclusions: Outpatient transition to XR-NTX using NTX/BUP was safe, well tolerated, and completed by most participants. Further studies with larger numbers of subjects are needed to see if this approach is useful for opioid detoxification and naltrexone induction.
Financial Support: Financial support and XR-NTX injections were provided through an Investigator-Initiated Trial Grant from Alkermes, Inc.

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MARIJUANA USE AND *FAAH* GENOTYPE PREDICT SLEEP QUALITY IN ADOLESCENTS AND EMERGING ADULTS.

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Aims: Marijuana (MJ) is the most commonly used illicit drug in the United States, with 31% of young adults (ages 19-28) endorsing use during 2012 (Johnston et al., 2012). Acute MJ use has been associated with decreased latency to fall asleep, yet MJ users still experience sleep problems such as reduced quality of sleep and increased awakenings (Schierenbeck et al., 2008; Cohen-Zion et al., 2009). The gene that codes for Fatty Acid Amide Hydrolase (*FAAH*) has been linked with both MJ use (Tyndale et al., 2007) and sleep quality (Huitron-Resendiz et al., 2004; Murillo-Rodríguez et al., 2011). Based on this evidence, we hypothesize that past year MJ use and *FAAH* genotype will be associated with reported sleep quality in adolescents and young adults.
Methods: Data were collected from 50 participants ages 18-25 (30M/20F); 27 were *FAAH* A carriers and 23 were of the homozygous (C/C) genotype. Exclusion criteria included psychiatric, major medical and neurologic disorders. Quantity and frequency of past year MJ use was assessed (Sobell & Sobell, 1992) and participants completed the Pittsburgh Sleep Quality Index (PSQI). Multiple regressions were used to predict PSQI total scores from past year MJ use, *FAAH* genotype, and their interaction after controlling for demographic variables.
Results: After controlling for ethnicity, age, and alcohol use, greater past year MJ use significantly predicted poorer sleep quality (p= .01). Furthermore, *FAAH* A carriers reported marginally better sleep quality than individuals with the (C/C) genotype (p= .13). No significant MJ**FAAH* interactions were found.
Conclusions: As predicted, we found that increased past year MJ use significantly predicted poorer sleep quality at the time of evaluation. This is consistent with previous studies indicating sleep abnormalities due to cannabis and THC use (Schierenbeck et al., 2008; Cohen-Zion et al., 2009; Gorelick et al., 2013). *FAAH* genotype only marginally predicted sleep quality; this is likely due to low power and additional studies are warranted. Clinical implications of MJ use in youth will be discussed.
Financial Support: 3R01DA030354; 1R03DA027457 (PI: Lisdahl)

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DRUG AND TOBACCO USE DURING PREGNANCY TRANSMIT GENETIC INFLUENCES ON DEVELOPMENTAL RISK FOR SUBSTANCE USE.

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Aims: Childhood behavior problems (incl. internalizing, INT) and dysregulated cortisol put children at risk for developing substance use problems (SU). We hypothesized that prenatal exposure to SU and INT would transmit genetic risk (birth mother [BM] lifetime SU and INT) and lead to higher child morning cortisol and more child INT over time. We tested whether genetic risk was associated with exposure to drugs, tobacco, alcohol, anxiety, and/or depression during pregnancy, and which prenatal risks mediated genetic influences on child cortisol and INT from 4.5 to 6 years.
Methods: We used an adoption design including 351 domestically adopted children, BM and adopted parents prospectively followed from birth.
Results: Structural equation model fitting results suggest that drug, alcohol, and tobacco use during pregnancy were associated with BM lifetime risk for SU, whereas anxiety and depression symptoms during pregnancy were associated with BM lifetime risk for INT. Prenatal tobacco and drug use during pregnancy were uniquely associated with higher morning cortisol in children, which was associated with fewer child INT at age 4.5 years and a reduction in child INT from 4.5 to 6 years.
Conclusions: Thus, drug use and tobacco use, the strongest prenatal risks, may increase youths' sensitivity to environmental cues (evidenced by increased morning cortisol). Whereas generally this sensitivity to environmental cues would translate into more problems in youth who would experience an environment consistent with the genetic and prenatal risk (i.e., parental SU), in this study children were adopted into generally positive environments. Thus, in this sample children exposed to drug and tobacco use may be able to take advantage of the generally positive environmental influences because of altered cortisol function.
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LONG-TERM PATTERNS OF HEROIN USE AND MENTAL HEALTH: 11-YEAR FOLLOW-UP OF THE AUSTRALIAN TREATMENT OUTCOME STUDY.

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Aims: Heroin dependence is a chronic and in many cases, lifelong condition, associated with comorbid mental health disorders. Using data collected as part of the Australian Treatment Outcome Study, the present paper aims to examine the major findings of heroin use, comorbid disorders and treatment patterns over 10-11 years.
Methods: 615 people with heroin dependence were recruited to the study in 2001-2002, and re-interviewed at 3-, 12-, 24-, 36-months and 10-11 years post-baseline (follow-up rates of 89%, 81%, 76%, 70% and 69% at the time of writing). Heroin dependence was assessed at each time point using the Composite International Diagnostic Interview version 2.1, and heroin treatment since the last interview was obtained using the timeline follow-back method.
Results: At 11-years, preliminary analyses indicate that over 14% of the cohort endorsed criteria for heroin dependence and 47% were in treatment for opiate dependence. One fifth of the cohort met criteria for current depression; 41% for current post traumatic stress disorder (PTSD); and 22% had committed at least one crime in the past month. The overwhelming majority of the cohort (98%) had experienced a period of abstinence in the follow-up period, with a median period of consecutive abstinence of 60 months (5 years). Overall, physical and mental health was poorer than population norms. Just over 10% of the cohort were deceased.
Conclusions: Despite significant reductions in heroin use and dependence over the 11-year follow-up period, there were continued high rates of other comorbidities. Further, although a significant proportion of the cohort achieved continual abstinence for substantial portions of the follow-up period, preliminary findings highlight the importance for long-term treatment for this chronic debilitating condition.
Financial Support: The study was funded by the Australian National Health and Medical Research Council.

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A MULTISITE RANDOMIZED CONTROLLED TRIAL OF MOTIVATIONAL ENHANCEMENT TREATMENT IN OUTPATIENT ADDICTION CARE CENTERS IN MEXICO.

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Aims: In Mexico, in the last decade there has been an increase in the population in need of treatment for substance use disorders, of which only a small percentage finishes treatment. Motivational Enhancement Treatment (MET) is a brief behavioral intervention that has shown to improve treatment outcomes through clinical trials in different populations, but not in Mexico. We hypothesized that with a Mexican sample of addiction treatment-seekers, MET would be more effective than Counseling as Usual (CAU) in reducing substance use and retaining clients in treatment.
Methods: 120 treatment-seekers (18-65 years) for any type of substance use from 3 outpatient addiction care centers were randomized to either MET or CAU treatment conditions. Outcome assessments were conducted at baseline, during and at the end of treatment phase, and at 1 and 2-month follow-ups. Primary outcome measures were self-reported number of days of substance use and of days of service use. Intervention effect was analyzed under an "intention to treat" approach.
Results: There was a significant difference in the patterns of means over time in level of substance use ($\chi 2$ (4) = 11.58, $p < .021$). There was not a significant difference in the patterns of means over time in level of services use ($\chi 2$ (3) = 0.74, $p < .8632$)
Conclusions: MET, when compared with CAU, has a moderate effect on treatment outcomes and is a promissory intervention considering it may have more lasting effects on substance use. A different approach has to be considered to enhance treatment retention in Mexican patients
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COCAINE-DEPENDENT SUBJECTS DISPLAY ATTENTIONAL BIAS TOWARD COCAINE-RELATED BUT NOT ALCOHOL-RELATED STIMULI.

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Aims: Cocaine dependence is characterized by heightened attentional bias towards cocaine related stimuli relative to neutral stimuli. One criticism of attentional bias measures is that cocaine users might be hypersensitive to all substance-related emotionally evocative stimuli and not specifically to cocaine-related stimuli. The aim of this study was to demonstrate that cocaine users display a larger attentional bias toward cocaine-related images than alcohol-related images.
Methods: Twenty-five cocaine dependent humans completed this within-subjects study that used a modified visual probe task. In this task, substance-related and matched neutral images were presented side-by-side. The substance-related images depicted cocaine or alcohol cues. Eye-tracking technology measured time spent fixating on each image. Cocaine cue and alcohol cue attentional bias scores were calculated as the difference in fixation time between the specific substance-related (i.e., cocaine or alcohol) and matched neutral images. Data were analyzed with repeated measures ANOVA.
Results: Subjects fixated on cocaine-related images significantly longer than matched neutral images but did not fixate on alcohol-related images longer than matched neutral images. The magnitude of the cocaine cue attentional bias score was significantly larger than the alcohol cue attentional bias score.
Conclusions: These data replicate previous findings showing that cocaine users display an attentional bias towards cocaine-related images. Importantly, these data demonstrate that cocaine cue attentional bias is not a result of a general hypersensitivity to substance-related emotionally evocative stimuli suggesting that cocaine cue attentional bias is the result of incentive salience produced by cocaine cue conditioning.
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DOPAMINE D3 RECEPTOR AVAILABILITY: SEX DIFFERENCES AND EFFECTS OF CHRONIC DRUG EXPOSURE.

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Aims: Chronic cocaine (COC) and methamphetamine (MA) exposure can cause neuroadaptations in the dopamine system, especially the D2-like superfamily, including the D3 receptor (DRD3) subtype. However, most studies have utilized male subjects. Recently, we found sex differences in the relationship between D2-like receptors and vulnerability to cocaine self-administration (SA). One aim of the present study was to determine the effects of quinpirole (QUIN), a preferential DRD3 agonist, in drug-naïve male and female rhesus monkeys. Next, we examined the effects of chronic COC (n=3) and MA (n=3) exposure on sensitivity to QUIN in male monkeys. Finally, using PET imaging with the radioligand [11C]PHNO, we examined the relationship between DRD3 availability and (1) QUIN-elicited yawning and (2) simple discrimination and reversal performance – a measure of cognitive flexibility.
Methods: Cumulative doses of QUIN (0.01 - 0.3 mg/kg) were injected i.m. in 30-min bins and the total number of yawns observed were recorded for each bin. QUIN-elicited yawning was characterized as an inverted U-shaped function of dose.
Results: Significant sex differences were noted with QUIN being less potent and eliciting fewer yawns in females. Additionally, monkeys with a MA SA history were more sensitive to the behavioral effects of low doses of QUIN vs. controls, whereas COC SA monkeys were not significantly different than controls. Finally, analyses revealed significant relationships between DRD3 availability and both QUIN-elicited yawning and acquisition of discrimination in several regions of the brain. Future studies will extend these results to females.
Conclusions: These findings suggest that QUIN-elicited yawning is an excellent tool for examining DRD3 activity, that this receptor is critical in discrimination learning, and that both sex and drug history influence individual sensitivity to the behavioral effects of DRD3 preferring compounds. Such information will be critical in developing sex-specific treatments for drug abuse.
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SEX AND HIV SEROSTATUS EFFECTS ON HIGH-RISK DECISION MAKING.

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Aims: Substance dependent individuals (SDIs) frequently make decisions guided by immediate reward rather than optimal future outcomes. Studies using the well-established Iowa Gambling Task (IGT) have shown that poor decision-making is more common among HIV+ compared with HIV-SDIs; and this vulnerability may be further increased among female HIV+ SDIs. In the present study, we investigated decision-making integrity in 144 SDIs using the Game of Dice Task, a measure of risky decision making with fewer cognitive demands than the IGT.
Methods: We tested 94 HIV+ and 50 HIV- individuals (28 and 41% female) using clinical interviews, questionnaires, and computerized cognitive tasks. All subjects were verified abstinent at testing. All subjects completed the Game of Dice Task, an 18-trial simulated gambling task. On each trial, the subjects must bet on the outcome of a dice throw. Information is provided about the likelihood and degree of monetary risk associated with each outcome.
Results: Data were analyzed by Sex x Serostatus analyses of variance and chi-square tests. There were no significant group differences in demographics, prevalence of DSM-IV diagnosed alcohol, cannabis, cocaine or opioid dependence or comorbid psychopathology. Women made significantly more risky choices on the GDT compared with men, $F(1,140) = 5.37$, $p < .05$, $d = .45$) but there were no significant Serostatus effects, $F < 1$.
Conclusions: We found no effect of HIV serostatus on GDT decision making but males significantly outperformed females. Compared with previous findings using the IGT, these data suggest that HIV+ SDIs show improved decision-making capacity with access to information about the outcome of their choices; but female SDIs persist in making poor decisions compared with males under these conditions. These results suggest the possibility of sex-specific impairment in reward-based decision-making.
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QUIT ATTEMPT PREDICTORS AMONG SMOKERS IN ADDICTION TREATMENT.

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Aims: To investigate factors predicting past quit attempts among smokers enrolled in substance abuse treatment in New York State.
Methods: Data were drawn from two prior cross-sectional surveys conducted among clients treated in 10 randomly selected substance abuse treatment programs. Among 820 clients recruited, 542 self-identified as current smokers, and 485 provided information about their quit attempts. The main outcome was reporting a serious quit smoking attempt in the past year, dichotomized as quit attempters or non-quit attempters. Univariate and multivariate logistic regression analyses were performed to explore predictors of attempting to quit.
Results: Quit attempters were more likely to receive tobacco-related services from their clinician (OR= 1.21; 95% CI: 1.01-1.46), to express positive attitudes about quitting (OR= 1.49; 95% CI: 1.11 - 1.99), and to report higher readiness to quit according to the stages of change model (for preparation OR= 2.31, 95% CI: 1.35 - 3.96; for contemplation OR= 2.93, 95% CI: 1.71 - 5.03).
Conclusions: Addressing patient attitudes about quitting smoking, having clinicians address smoking in the course of addiction treatment, and offering interventions to increase readiness to quit may contribute to increased quit attempts in smokers enrolled in addiction treatment programs.
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TRENDS IN RACIAL/ETHNIC DIFFERENCES IN HEROIN USE AND HEROIN RISK BEHAVIORS AMONG NONMEDICAL USERS OF PRESCRIPTION OPIOIDS FROM 2002 TO 2011.

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Aims: To examine changes in the patterns of past-year heroin use and heroin risk behaviors (injection drug use and abuse/dependence) among Whites, Blacks, and Hispanics who were nonmedical users of prescription opioids (POs).
Methods: Secondary analysis of the US National Survey of Drug Use and Health (NSDUH) 2002-2005 and 2008-2011 data using weighted logistic regression models, stratified by race/ethnicity and adjusted for other socio-demographics, frequency past-year of PO use (1-29 days, 30-99 days, 100+ days) and other past-year drug use.
Results: Among PO users, there was a significant increase in past-year heroin use across time, from 18.53 per 1000 in 2002-2005 to 35.57 per 1000 in 2008-2011 ($p<0.01$). This increase was mainly due to an increase in past-year heroin use among White (from 21.30 per 1000 in 2002-2005 to 38.73 per 1000 in 2008-2011, $p<0.01$) and Hispanic (from 11.56 per 1000 in 2002-2005 to 26.04 per 1000 in 2008-2011, $p=0.05$) nonmedical PO users. There was a significant increase in heroin use among Blacks, but only among those that used PO at least 30 days in the past-year. White past-year PO users who used PO at least 30 days in the past-year were more likely to have ever injected heroin and POs, to meet criteria for heroin and PO abuse/dependence, and think heroin was fairly easy to obtain, compared to those who used POs less than 30 days a year. Black and Hispanic past-year PO users who used POs 100 or more days a year were more likely than those that used PO less than 30 days in the past-year to be injection heroin users, have heroin abuse/dependence and report that heroin was fairly easy to obtain.
Conclusions: Changes in the patterns of heroin use and heroin risk behaviors across time among nonmedical users of PO vary by race/ethnicity. Across all racial groups, frequent PO users are at greatest risk of heroin use and related harms and should be the focus of harm reduction and substance abuse treatment interventions.
Financial Support: RO1HD060072 (Martins), KO1DA030449 (Cerdá), R21AA021909 (Cerdá).

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EVALUATION OF SEX DIFFERENCES IN CANNABINOID WITHDRAWAL IN RATS.

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Aims: Although epidemiological studies indicate that cannabis using women attempting to quit report more withdrawal and relapse compared to men, only a handful of empirical studies have examined sex differences in cannabinoid dependence. The purpose of the study was to examine sex differences in withdrawal from Δ9-tetrahydrocannabinol (THC) in a rat model.
Methods: Forty male and forty female Sprague-Dawley rats were administered THC or vehicle twice daily for 6.5 days. Locomotor activity, temperature, and warm water tail withdrawal were assessed on days 1 and 6. On the afternoon of day 7, rats were administered a vehicle or rimonabant challenge, counterbalanced across subchronic dosing groups, followed by assessments of locomotor activity, temperature, tail withdrawal, acoustic startle, and observation of withdrawal related behaviors.
Results: Male rats, but not females, showed THC-induced locomotor decreases on day 1, and developed tolerance to this effect across days. Female rats administered THC and challenged with rimonabant showed increased retropulsion compared to male and female rats in other treatment groups. Subchronic treatment with THC followed by rimonabant challenge increased paw tremors and head twitches, decreased prepulse inhibition, and led to a lack of locomotor habituation in rats of both sexes. Rats in all groups treated with THC exhibited increased startle amplitude and weight loss.
Conclusions: This study represents the first systematic examination of THC dependence in gonadally intact adult rats of both sexes, extends findings reported previously only in male rodents to females, and revealed some sex differences. The results suggest that the changes that occur during antagonist-precipitated withdrawal from THC extend beyond the typically reported somatic signs to more nuanced disruptions of cognitive and affective functioning. The breadth of withdrawal signs observed in rodents mirrors those that have been observed in humans.
Financial Support: NIDA Grant DA-016644.

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AGE OF CIGARETTE SMOKING ONSET IS ASSOCIATED WITH P300 SMOKING CUE REACTIVITY: PRELIMINARY EEG FINDINGS.

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Aims: The typical age range for initiating smoking and developing long-term nicotine dependence, ages 15-18, coincides with critical neuromaturation. Thus, early onset (age<16yrs), relative to late onset (age>16yrs), smoking may be particularly noxious for developmentally immature systems that regulate neural signaling efficiency and reactivity. The current study investigates effects of age of smoking onset on alterations in neurophysiological measures of smoking cue reactivity and subjective craving in adult smokers.
Methods: Adult early onset smokers (EOS; n=4) and late onset smokers (LOS; n=7) in acute withdrawal, as well as adult non-smokers (NS; n=6) took part in an ongoing electroencephalography (EEG) smoking cue reactivity study. Participants handled neutral objects as well as smoking-related objects, and also viewed two computerized presentations of smoking, neutral, or arousing stimuli in an oddball paradigm. P300 event-related potentials were measured during picture presentations, and craving/mood assessments and physiologic recordings also were collected.
Results: Preliminary findings indicate significantly higher P300 amplitudes in the central midline (Cz) channel in EOS, LOS and NS in response to drug images ($p<0.02$), but not neutral or arousing images, after handling smoking objects. Furthermore, P300 amplitudes trended towards being higher in LOS in response to drug images ($p=0.06$) compared to EOS and NS groups. EOS and LOS reported greater craving ($p=0.05$) after handling smoking objects relative to after handling neutral objects.
Conclusions: Greater P300 reactivity was associated with smoking cues, particularly in LOS. Differential P300 reactivity profiles between LOS and EOS may be related to differences in compensatory signaling neuroadaptations resulting from smoking during early maturation. Preliminary findings suggest that late onset smoking may alter neurophysiological signaling systems involved in responding to smoking-related pictures, which could have important implications for designing smoking cessation interventions.
Financial Support: NIDA K01 grant DA034028 (YM)

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UNDERSTANDING THE SERVICE NEEDS OF ASSAULT-INJURED, DRUG-USING YOUTH PRESENTING FOR CARE IN AN URBAN EMERGENCY DEPARTMENT.

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Aims: To inform optimal content/location of violence interventions, it is critical to understand the baseline characteristics, and intent to retaliate, of drug using assault-injured youth
Methods: At an urban ED, assault-injured (AI) youth (ages 14-24) endorsing past 6 month substance use (n=350), and a proportionally-sampled substance using comparison group (CG) presenting for non-assault-related care (n=250) were recruited, completed a baseline assessment (participation rate 82%). Medical chart review was conducted. Conditional regression analysis was conducted to examine correlates associated with seeking ED care for an assault injury
Results: Over half (57%) of all youth (58.8% male, mean age 20.1, 58.2% African American) met criteria for drug/alcohol use disorder (9% receiving prior treatment). Among the AI group, 1/4 intended to retaliate (of which 49% had firearm access). The AI youth report poorer mental health (PTSD), more substance use, and were more likely to report prior ED visits for assault or psychiatric evaluation. Regression analysis found AI youth were more likely to be on probation/parole (AOR=2.26; CI=1.28, 3.90), and have PTSD (AOR=1.88; CI=1.01, 3.50) than the CG
Conclusions: AI youth have substantial unmet needs for substance use and mental health treatment including PTSD. These characteristics along with increased risk of retaliation, increased ED service utilization, and firearm access highlight the need for interventions that start at time of ED visit
Financial Support: NIDA RO1 024646 & CDC U01 CE001957

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DEVELOPMENT AND PILOT TESTING OF AN ONLINE TRAINING TO RAISE AWARENESS AMONG CRIMINAL JUSTICE PROFESSIONALS OF MEDICATIONS USED TO TREAT OPIOID ADDICTION.

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Aims: We developed and tested an online training for criminal justice professionals to raise their awareness of the potential benefits that medication assisted treatment of opioid addiction (MAT) has for the people they serve.
Methods: Through two pilot studies, we examined to what extent the training increased criminal justice system treatment referrers' and decision makers' (1) knowledge of MAT, (2) positive attitudes toward MAT, and (3) willingness to refer criminal justice clients to MAT services. In study one, 45 treatment referrers participated in a randomized trial of the training. In study two, 25 decision makers participated in a pre/post-trial of the training. Paired t-tests and repeated measures mixed effects models were used to test hypotheses that participation in the training would increase knowledge, positive attitudes, and willingness to refer to MAT.
Results: (Study 1) At post-training, the experimental group had significantly higher scores than those in the control group on knowledge items and on all measures assessing attitudes towards MAT and willingness to refer to MAT. Effects sizes (d) ranged from .66 to 1.03. Mixed effects models indicated significant group effects for items assessing whether medications should be used more often and items assessing general attitudes towards MAT. (Study 2) Significant increases at posttest, in the desired direction, were observed on four of the five dependent variables. Effect sizes (d) at posttest ranged from 0.53 to 1.16.
Conclusions: Results from these studies provide preliminary support for the efficacy of our online MAT training in improving treatment referrers' and decision makers' perceptions of MAT.
Financial Support: This study was supported by a grant from the Pennsylvania Department of Health (SAP #4100054873).

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INITIATION OF NONMEDICAL PRESCRIPTION OPIOID USE AND DEVELOPMENT OF OPIOID DEPENDENCE AMONG YOUNG ADULTS.

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Aims: To elucidate the social contexts in which youth initiate nonmedical prescription opioid (PO) use, their motivations for initiation, and the processes leading to opioid dependence and associated negative health consequences.
Methods: Forty-four New York City young adults (ages 18-32) who reported nonmedical PO use in the past 30 days were recruited for digitally audiotaped, 1.5-hour-long, semi-structured interviews. Interviews focused on motivations for and contexts surrounding initial PO use, drug use trajectories and practices, and evolving perceptions of POs versus heroin. Interview data were transcribed and content analyzed for key themes.
Results: Mean age of PO-use initiation was 16.8 years. Most initiated PO use in a recreational context with high school peers as part of a poly-substance/poly-pharmaceutical use pattern. At the time of initiation, POs were viewed as safer, less stigmatized, and less addictive than illicit street drugs. Initiation was facilitated by ready, cost-free access to POs from household sources. As PO use escalated and, for many, opioid dependence developed, difficulties in accessing and affording enough POs to forestall withdrawal led 73% (32/44) to experiment with or transition to heroin use, typically via injection, within two years of PO initiation (mean age: 18.3 years). Of the 33 subjects who reported on treatment experiences, 76% (25/33) had received some treatment, most commonly methadone maintenance (36%; 12/33) and inpatient rehabilitation (30%; 10/33). Eighteen percent (6/33) report buying methadone or buprenorphine on the street for self-treatment.
Conclusions: Results suggest that a subset of young adults who initiate nonmedical PO use as teens develop opioid dependence which can motivate them to seek more cost-effective means of maintaining their habits (i.e., transition to heroin and/or injection drug use). There is a pressing need to develop innovative prevention programs to help younger teens avoid initiating nonmedical PO use and to assist current PO users in preventing escalation to riskier forms of opioid use.
Financial Support: Supported by NIDA grant# R01DA035146

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ASSOCIATIONS BETWEEN GRAY MATTER VOLUME, SMOKER STATUS, AND SMOKING HEAVINESS.

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Aims: Smokers, as compared to nonsmokers, exhibit less gray matter volume (GMV) in several brain regions. In the current study, we sought to replicate and extend the extant literature by examining within-group differences in smokers that are associated with GMV.
Methods: Voxel Based Morphometry (VBM) with DARTEL was conducted on anatomical data from several studies of smokers (n=110) and nonsmokers (n=79). A mask of between subjects differences in GMV, controlling for age and gender ($p<.05$; $k \geq 218$), was then used to examine relations between GMV and baseline self-report measures among smokers. We assessed smoking heaviness through two indicators: years smoking and nicotine dependence, measured by FTND total score.
Results: There was a significant positive association between years smoking and FTND score ($p=.047$). As expected, we found smokers to have significantly less GMV throughout the cortex and thalamus. Next, we examined years smoking and FTND score as predictors of GMV among smokers. Years smoking was negatively correlated with GMV in superior frontal gyrus (SFG). FTND was negatively correlated with GMV in medial prefrontal cortex (mPFC) and dorsal anterior cingulate (dACC).
Conclusions: Findings provide cross-validation for lower GMV among smokers vs. nonsmokers. Among smokers, indices of smoking heaviness were differentially correlated with GMV in particular brain regions. While years smoking was negatively correlated with GMV in SFG, nicotine dependence was negatively associated with GMV in mPFC and dACC—critical nodes of the emotional appraisal circuit. Findings provide key information about the relationship between smoking and a subset of brain regions, and will be interpreted in light of associations with smoking motives.
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ATTENUATION OF METHAMPHETAMINE-INDUCED STRIATAL NEUROTOXICITY INVOLVES BOTH NEURONAL AND GLIAL MECHANISMS.

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Aims: Neurotoxic exposure to methamphetamine (METH) activates a variety of neuronal and glial mechanisms. Sigma receptors are found in both neurons and glia, and have been targeted to reduce cytotoxicity and inflammation in select disease states. Therefore, the purpose of this study was to determine whether the sigma receptor putative antagonist SN79 could mitigate changes in select striatal neuronal and glial processes resulting from neurotoxic exposure to METH.
Methods: Male, Swiss Webster mice were treated with a neurotoxic regimen of METH in the absence or presence of pretreatment with SN79. The brains were collected at various time points and striatal samples evaluated for drug-induced changes using immunohistochemistry or fluorescence, real time PCR, and Western blots.
Results: SN79 pretreatment significantly attenuated the following METH-induced deficits in striatal neurons: dopamine and serotonin transporter expression, apoptosis. SN79 pretreatment also attenuated METH-induced M1 microglial activation and increases in proinflammatory cytokine mRNA expression (il-6, lif, osm) in the striatum. METH also induced astrogliosis through the activation of JAK2/STAT3 signaling, with SN79 pretreatment preventing the following METH-induced increases in the striatum: GFAP mRNA and protein expression, OSMR expression, phosphorylation of STAT3 (Tyr-705).
Conclusions: Together, the data indicate that sigma ligands such as SN79 can convey protective effects against METH by targeting both neuronal and glial processes.
Financial Support: National Institutes of Health (R01 DA013978, R01 DA023205, R01 NS061954, T32 GM081741)

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OREXIN/HYPOCRETIN IN THE PARAVENTRICULAR NUCLEUS OF THE THALAMUS MEDIATES COCAINE-SEEKING BEHAVIOR IN RATS.

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Aims: Growing evidence implicates a role for orexin/hypocretin (Orx/Hcrt) neurons that originate in the lateral hypothalamus (LH) and project to the paraventricular nucleus of the thalamus (PVT) in drug addiction. Our working hypothesis is that cocaine-induced dysregulation of the Orx/Hcrt system modifies Orx/Hcrt-PVT transmission, an effect that is long-lasting. The aim of this study was to evaluate the influence of cocaine access on Orx/Hcrt-induced cocaine seeking and compare it with behavior motivated toward a highly palatable conventional reinforcer, sweetened condensed milk (SCM).
Methods: One hundred fifty-six male Wistar rats were trained to self-administer short-access cocaine (ShA; 2 h/day), long-access cocaine (LgA; 6h/day), or SCM (30 min/day) and then subjected to daily extinction (2h/day) training. The day after, the rats received intra-PVT microinjections of Orx-A/Hcrt-1 (0, 0.25, 0.5, 1, and 2 μg) and then placed into operant chambers under extinction conditions.
Results: The effects of Orx-A/Hcrt-1-induced reinstatement on cocaine seeking in the ShA group were characterized by an inverted U-shaped dose-effect function, with low doses but not high doses eliciting reinstatement. In contrast, Orx-A/Hcrt-1 induced reinstatement in the SCM group at high but not low doses. A leftward shift in the Orx-A/Hcrt-1 dose-effect function was observed for the reinstatement of ShA cocaine seeking compared with SCM seeking. Additionally, Orx-A/Hcrt-1-induced reinstatement in the LgA group produced a left-upward shift of the dose-response function compared with SCM group and an upward shift compared with the ShA group.
Conclusions: These findings suggest that a history of cocaine dependence leads to neuroadaptive changes at the level of the PVT, resulting in "sensitization" of LH-PVT-Orx/Hcrt transmission, reflected by increased sensitivity (i.e., a leftward shift) and exacerbated behavioral responses (i.e., an upward shift) to the to the effects of Orx-A/Hcrt-1.
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CAREGIVER AND YOUTH ENGAGEMENT IN MANDATED JUVENILE DRUG TREATMENT: INFLUENCE ON SUBSTANCE USE.

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Aims: We assessed the association between youth and caregiver engagement in Risk Reduction Treatment for Adolescents (RRTA) and youth 3- and 6-month substance use. We hypothesized that high engagement in RRTA, an office-based intervention that includes contingency management (CM), would be associated with greater reductions in youth substance use.
Methods: Data were obtained from 42 youth-caregiver dyads in the RRTA arm of an RCT in two juvenile drug courts. Engagement was measured using the Family Engagement Therapist Adherence Measure (FETAM), collected monthly via separate youth/caregiver phone interviews. Based on the data distribution, FETAM scores were dichotomized into high or low engagement at both the middle (month 3) and before the end (month 5) of treatment. Self-reported substance use (Timeline Follow-Back) and urine drug screens (UDS) were assessed at 3 and 6 months. Logistic regression estimated the longitudinal effect of RRTA on youth substance use. Fisher's exact tests measured the cross-sectional association between youth and caregiver engagement and youth substance use at 3- and 6-months.
Results: At baseline, 67% of participants actively used substances. There was a significant reduction in self-reported substance use (3-mo.=26%; 6-mo.=15%) and UDS (3-mo.=10%; 6-mo.=11%) by 6 months ($p's<0.05$). At 3 months, 54% of caregivers and 47% of youth were highly engaged; this decreased to 44% and 38% at 5 months, respectively. High caregiver and youth engagement were significantly associated with youth substance use abstinence at 3 months ($p's<0.05$), not 6 months.
Conclusions: High youth and caregiver engagement in RRTA appears to have accelerated reductions in substance use early in treatment; substance use continued to decline for all RRTA participants through the end of the intervention. Future studies should explore the association between other RRTA components (e.g. CM) and treatment outcomes.
Financial Support: This study was supported by grants R01DA025880 and T32DA007292 from the National Institute on Drug Abuse.

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IMPACT OF HEAVY DRINKING AMONG DRUG USERS IDENTIFIED BY SCREENING IN PRIMARY CARE.

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Aims: Unhealthy alcohol use is common among drug users, but little information is available on its effect in patients who screen positive for drugs in primary care. We aimed to study heavy drinking in such patients, and hypothesized that it would be associated with more severe drug use.
Methods: We examined a cohort of patients in an urban primary care setting with an Alcohol Smoking and Substance Involvement Screening Test (ASSIST) drug score of ≥2. The main independent variable was ≥1 heavy drinking day (HDD) in the past month at baseline. The primary outcome was defined as the number of days use of drug of most concern (DOMC) in the past month, assessed at 6 months; secondary outcomes included drug dependence, injection drug use (IDU) and use of >1 drug at 6 months. Multivariable logistic and negative binomial regression models controlled for potential confounders.
Results: Of 589 primary care patients screening positive for drug use (68% male, 63% African American), 48% had at least one HDD and 16% had an ASSIST score of 27+ consistent with drug dependence. Baseline HDD was negatively associated with number of days use of the DOMC at 6 months (IRR 0.75, 95% CI [0.62 – 0.91]), but positively associated with drug dependence (OR 1.77, 95% CI [1.10-2.84]) and use of more than one drug (OR 1.73, 95% CI [1.17-2.55]). No association was detected for IDU (OR 1.26, 95% CI [0.50-3.22]).
Conclusions: Heavy drinking is common among primary care patients who screen positive for drug use. One or more HDD was significantly associated with fewer days use of DOMC, and a higher odds of dependence and use of >1 drug at follow-up. The apparent negative association between HDD and days use of DOMC could be explained by the use of >1 drug, or by alcohol use as a replacement. These findings suggest that assessing for heavy drinking among drug users identified by screening in primary care may yield clinically useful information.
Financial Support: Secondary analysis of ASPIRE trial data, funded by NIDA 1 R01 DA025068 with support from SAMHSA

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SEX DIFFERENCES IN DEPRESSIVE-LIKE EFFECTS OF KAPPA OPIOID RECEPTOR ACTIVATION IN RATS.

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Aims: In males, cocaine increases dynorphin expression in reward-related brain regions. Upon drug cessation, effects of dynorphin at kappa opioid receptors (KORs) are unmasked, contributing to withdrawal-induced negative affective states and relapse. We showed that female rats are less sensitive than males to depressive-like effects of the KOR agonist U50,488 using intracranial self-stimulation (ICSS), suggesting sex differences in the role of dynorphin in cocaine dependence. The aim of this study is to further examine sex differences in KOR-mediated modulation of affective state.
Methods: Adult male and female Sprague Dawley rats (n=8-10/group) were group housed or socially isolated for 5 weeks as an ethologically relevant stressor. Effects of social isolation on sensitivity to U50,488-induced conditioned place aversions and anxiety-like behavior in the elevated plus maze (EPM) were measured. Separate rats (n=6/group) were used to quantify levels of dynorphin and KOR mRNA using qRT-PCR in reward-related brain regions.
Results: Group housed males showed a significant place aversion to U50,488 at only one dose (2.5 mg/kg), whereas U50,488 produced place aversions in females at all doses tested (1.25 – 10.0 mg/kg). Social isolation stress selectively occluded U50,488 (2.5 mg/kg)-induced conditioned place aversions in males but had robust anxiogenic effects in both sexes in the EPM. Females had higher levels of dynorphin mRNA in the bed nucleus of the stria terminalis (BNST) and paraventricular nucleus of the hypothalamus (PVN) compared to males, but lower levels of KOR mRNA in the BNST.
Conclusions: Taken together, these data suggest that although KOR activation is less aversive in females (ICSS), it produces stronger negative associations (place conditioning). Additionally, there is a fundamental sex difference in KOR function at the molecular level that may modulate responses to stressors like social isolation. This has important ramifications for understanding sex differences in cocaine addiction.
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GENDER DIFFERENCES IN LABORATORY STRESS RESPONSE AMONG PRESCRIPTION OPIOID-DEPENDENT INDIVIDUALS.

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Aims: To examine gender differences in subjective and physiologic response to a laboratory stressor among men and women with current prescription opioid dependence (POD). Based on findings from non-POD populations, we hypothesized that female PODs would demonstrate increased subjective and physiologic stress response as compared to male PODs.
Methods: Participants (N=39) met DSM-IV-TR criteria for current POD and were recruited from the community. POD was assessed using the SCID. Outcomes included: (1) self-reported visual analog scale ratings of stress, craving, pain, affect, ability to resist using, and market value willing to pay; and (2) peak heart rate, peak galvanic skin response (GSR), and mean arterial pressure (MAP). Outcomes were assessed immediately following randomization and exposure to either the Trier Social Stress Test (TSST; n=19) or no-stress control (no stress; n=20).
Results: Women demonstrated significantly greater self-reported stress [$F(1,35)=11.24$, $p<.01$], craving [$F(1,35)=4.54$, $p<.05$], and sadness [$F(1,35)=41.00$, $p<.01$]. No gender differences emerged on physiologic outcomes. As expected, significant group (TSST vs. no stress) differences emerged in self-reported stress [$F(1,35)=41.77$, $p<.001$], anger [$F(1,35)=13.00$, $p<.001$], sadness [$F(1,35)=4.78$, $p<.05$], and MAP [$F(1,35)=5.28$, $p<.05$], such that the TSST group was more reactive demonstrating effectiveness of TSST. No significant interactions between gender and stress group were found.
Conclusions: Whereas men and women's physiologic response to an acute laboratory stressor were statistically equivalent, subjective experience of stress, craving, and negative mood were more pronounced among women. The findings indicate a potential enhanced susceptibility to stress-induced craving among women with POD. Future research should explore if a heightened stress response among women is related to gender differences in PO initiation, maintenance and relapse.
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AN OPEN-LABEL PILOT TRIAL OF N-ACETYLCYSTEINE AND VARENICLINE IN CIGARETTE SMOKERS.

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Aims: Varenicline (VAR) has demonstrated superior efficacy over other smoking cessation pharmacotherapies, yet 12 week cessation rates only reach 40-45%. Preclinical literature suggests that nicotine dependence pharmacotherapies should target the glutamatergic system. N-acetylcysteine (NAC) restores normal glutamate signaling, making it an attractive candidate. NAC and VAR together may promote abstinence at higher rates than with either medication alone. No prior studies have assessed the safety and feasibility of their co-administration.
Methods: Participants (N=10) were cigarette smokers interested in reducing or quitting smoking (recruitment ongoing). They received 4 weeks of open-label treatment with NAC (2400 mg twice daily) and VAR (2.0 mg twice daily, following standard titration) and were assessed weekly for adverse events (AEs) and reductions in smoking. Mean age of the sample was 31 (22-46) yrs old, 70% female and 60% Caucasian. Participants smoked an average (SD) of 17 (10) cigarettes per day.
Results: A total of 21 AEs were reported across eight participants. The majority of AEs were mild (90%) and no action was required (90%). The most commonly reported AE was increased appetite. One participant reduced VAR dose due to AEs (insomnia and irritability), which resolved with dose reduction. Medication adherence (self-reports and pill counts) was excellent (99%). Additionally, reductions in cigarettes per day were reported from 16.3 (10.6) at study enrollment to 5.0 (4.1) at the end of treatment ($p<.003$).
Conclusions: These preliminary data provide the first demonstration of safety and feasibility of the co-administration of NAC and VAR in cigarette smokers. The prevalence of AEs was low and no participants terminated medication. Reductions in smoking are interpreted cautiously given the lack of control group, but these data support future research on NAC and VAR as a combined pharmacotherapy for smoking cessation.
Financial Support: NIDA grants P50DA015369 (PI Kalivas) and U01DA031779 (PI Gray).

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THE IMPACT OF STATE MEDICAL MARIJUANA LEGISLATION ON ADOLESCENT MARIJUANA USE.

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Aims: The objective of this study was to assess the impact of medical marijuana legalization across the United States by comparing trends in adolescent marijuana use between states with and without legalization of medical marijuana.
Methods: The study utilized data from the Youth Risk Behavioral Surveillance Survey (YRBS) between 1991 and 2011. States with a medical marijuana law for which at least two cycles of YRBS data were available before and after the implementation of the law were selected for analysis. Each of these states was paired with a state in geographic proximity that had not implemented the law. Chi-squared analysis was used to compare characteristics between states with and without medical marijuana use policies. A difference-in-difference regression was performed to control for time-invariant factors relating to drug use in each state, isolating the policy effect, then calculated the marginal probabilities of policy change on the binary dependent variable.
Results: Across years and states, past-month marijuana use was common (20.9%, 95% CI, 20.3-21.4). There were no statistically significant differences in marijuana use before and after policy change for any state pairing. In the regression analysis, we did not find an overall increased probability of marijuana use related to the policy change (marginal probability, 0.007, 95% CI -0.009, 0.02).
Conclusions: This study did not find increases in adolescent marijuana use related to legalization of medical marijuana.
Financial Support: This work was supported by a grant from the Rhode Island Medical Foundation

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INTENDING TO QUIT SMOKING IS ASSOCIATED WITH FRONTOSTRIATAL GREY MATTER VOLUME VARIATION.

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Aims: MRI studies report brain GMV differences in smokers relative to non-smokers in frontostriatal circuitry — regions implicated in dysregulated affect and behavior. While the striatum plays a major role in both reward processing and addiction, frontal cortical regions are associated with top-down control and behavioral inhibition. Prior clinical studies demonstrate that frontostriatal volume varies as a function of smoking history, but little is known about the relation between GMV differences and quit intentions. Thus, the aim of this study was to explore these relationships using VBM.
Methods: Anatomical data aggregated from several samples of smokers involved in a smoking cessation study (n = 53) or non-quit studies (n = 48) were analyzed. Baseline nicotine dependence (FTND) and depressive symptoms (CES-D) were assessed. Age, sex, depression and years smoking were covaried. A whole-brain correlation and three ROI (caudate, putamen, and nucleus accumbens [NAcc]) analyses were entered into independent one-way ANOVAs to examine group differences in mean volumetric data.
Results: Groups did not significantly differ in FTND. Smokers who were motivated to quit exhibited more GMV in bilateral putamen, left caudate, left NAcc and right IFG (Z's >2.9). No GMV regions were identified for unmotivated > quitting-motivated smokers. Finally, left NAcc volume was negatively correlated with FTND only among smokers intending to quit.
Conclusions: Greater striatal GMV observed in smokers with an intention to quit may indicate a greater presence of dopaminergic neurons; thus, increased potential for behavioral flexibility and restructuring reward learning. Findings will be discussed within the context of interventions that aim to remediate dysregulated reward circuitry function and reduce nicotine dependence.
Financial Support: This study was supported by the following grants: DA026536 (Froeliger); DA025876, DA023516 (McClernon).

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DO CHIEF COMPLAINTS ALLOW TARGETING OF SBIRT IN THE EMERGENCY DEPARTMENT?

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Aims: ED-based SBIRT for alcohol and drug use has the potential to impact public health greatly. Time and resource constraints limit implementation. Targeted intervention may be more efficient and practical. We hypothesized that we could use chief complaints to identify patients at highest risk of positive drug or alcohol use assessments.
Methods: Using baseline data from NIDA CTN0047: SMART-ED, free text chief complaints of 14,972 subjects from six sites were coded using a tested algorithm (Thompson, 2006). Multiple team members manually reviewed and further collapsed the chief complaint categorization to ensure agreement. We excluded subjects having missing data or complaints related to substance use and chief complaints stated by <15 subjects. Positive screens were defined as AUDIT-C >4 for men and >3 for women (alcohol) and DAST>2 (drugs). We ranked-ordered the chief complaints by their sensitivity and positive predictive value to 1) minimize the number of chief complaints and 2) assess the fewest number of ED patients. Our goal was to identify 75% of ED patients having positive assessments using these strategies.
Results: The screening assessments were positive in 5,805/14,561(39.9%) for alcohol and 2,454/14,494 (16.9%) for drugs. We collapsed the free-text chief complaints into 50 usable categories. To identify 75% of all ED patients having positive assessments using the first strategy would require including 19 chief complaints for alcohol screening and 20 chief complaints for drug screening. Adapting the second strategy, we would need to screen at least 71% and 68% of all ED patients for alcohol and drugs respectively to identify 75% of those having positive assessments.
Conclusions: Based on this large, multicenter study, chief complaints provide little assistance in targeting SBIRT for alcohol or drug use in the ED.
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USING THE VACS INDEX TO TRACK HEALTH OUTCOMES ASSOCIATED WITH ABSTINENCE AMONG HIV-INFECTED PATIENTS RECEIVING OPIOID AGONIST TREATMENT.

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Aims: Opioid abstinence observed during opioid agonist treatment (OAT) may result in improved health, especially among HIV-infected individuals (HIV+). The Veterans Aging Cohort Study Index (VI) includes measures of age, liver, kidney, hematologic function, Hepatitis C status, CD4 count and HIV viral load to create a validated biomarker reflecting overall health in HIV+. A >4 point increase in the VI is associated with a >15% increase in 5 year mortality. We assessed the association between opioid abstinence and the VI among HIV+ participants receiving OAT.

Methods: HIV+ participants initiating OAT between 2000 and 2011 were identified. Eligible participants had a VI score within a year prior to initiating OAT, a VI score between 6 weeks and 1 year after OAT initiation, and at least 1 urine toxicology analysis in the 6 week interval prior to a VI score. Abstinent intervals had no positive urines in the 6 weeks preceding each VI score. Non-abstinent intervals had >1 opioid positive urine during the 6 weeks preceding each VI score. We assessed the association between non-abstinent intervals and VI scores with linear mixed models using a univariate model and a multivariate model that adjusted for pre-treatment VI score. Participant was specified as a random effect to account for multiple observations per participants.

Results: We identified 494 participants who met eligibility criteria. Mean age was 53 years, 99% were male, 20% white, 72% African-American, and 8% Hispanic. Fifteen percent initiated buprenorphine; 85% methadone. Based on univariate models, VI scores during non-abstinent intervals were higher by a mean of 4.3 points compared to abstinent intervals (p=.007). In the multivariate model, VI scores during non-abstinent intervals were higher by a mean of 2.8 points compared to abstinent intervals (p=.024).

Conclusions: Ongoing opioid use during OAT appears to be associated with worse VI scores. The VI may serve as a useful biomarker to reflect the health benefits of efficacious drug treatment.

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ETHANOL METABOLISM IN NEURAL STEM CELLS.

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Aims: Neural stem cells (NSCs) are a sub-population of cells in the adult brain responsible for neurogenesis. Proliferation and differentiation of NSCs is tightly regulated by a number of genetic and environmental factors. These regulatory factors help ensure a healthy balance of neuronal and glial cells. This balance is critical in brain functions involving injury recovery, learning, and memory. Chronic alcohol abuse is a global public health concern, in part for its affiliated neurological disorders. NSC proliferation and differentiation has been shown to be affected by excessive alcohol consumption, which may result in neural damage, reduced capacities of NSCs for repair, and alteration of homeostasis in certain brain regions. The mechanism through which alcohol contributes to changes in NSCs is still unknown. My central aim was to elucidate the mechanism through which neural stem cells metabolize and adapt to ethanol exposure.

Methods: I employed an in vitro cell culture model of chronic ethanol exposure by culturing human neural stem cells and performing a dose-response treatment with different concentrations of ethanol. At the terminus of the experiment, whole cell lysates were harvested and western blot analysis was performed to measure abundance of ethanol metabolizing enzymes.

Results: I have found that ethanol treatment in vitro results in altered expression of enzymes responsible for ethanol metabolism in human neural stem cells.

Conclusions: These findings provide insights into the metabolic adaptation of NSCs following ethanol exposure, and indicate the importance of further investigation to enhance NSC-mediated neural repair after alcohol abuses.

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ANXIETY SENSITIVITY AND THE DISCREPANCY BETWEEN MOTIVATION TO CHANGE AND PERCEIVED ABILITY TO CHANGE.

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Aims: Anxiety sensitivity (AS)—the fear of sensations associated with anxiety—is associated with barriers to change among smokers and with treatment dropout in patients with illicit drug use disorders. However, little is known about how AS is related to engagement in treatment. We hypothesized that AS would be associated with reduced confidence in the ability to change (e.g., in the context of physical and affective symptoms of early abstinence), even among those with high levels of motivation. Given gender differences in AS and its relationship to outcomes, we examined the impact of gender on this relationship.

Methods: Consecutive patients admitted to an inpatient substance use disorder treatment program were offered the opportunity to participate in a brief cross-sectional study. Participants completed a battery of self-report measures examining substance use, anxiety, and treatment motivation.

Results: The sample consisted of 144 participants (44 females). Women reported higher AS relative to men at a trend level ($t = 1.82$, $p = .07$). Participants with higher AS reported more days of heavy alcohol use ($r = .18$, $p < .05$) and benzodiazepine use ($r = .21$, $p < .05$) and greater functional impairment in psychiatric, social, and occupational domains (all $ps < .05$). The sample as a whole reported very high motivation to change (mean = 9.25 out of 10); however on average, participants reported only moderate confidence in their ability to remain abstinent in the next month. When controlling for motivation to change, days of alcohol and drug use, anxiety, and craving, AS was significantly associated with lower confidence in remaining abstinent among men, but not women.

Conclusions: These results are consistent with previous studies suggesting differences in the impact of AS on substance use disorders between men and women. Interventions targeted at reducing AS may enhance patient beliefs in their ability to change, which has been shown to be an important predictor of treatment outcome.

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WEB-BASED MEDICAL SCHOOL EDUCATION ON SUBSTANCE USE DISORDERS.

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Aims: The implementation of the ACA and the Parity Acts have elevated the importance of training physicians to effectively identify and manage substance use disorders. The Betty Ford Institute and the Treatment Research Institute have created a 12-lecture, on-line course for medical students that also includes virtual medical cases and preparation for course instructors.

The course is pre-clinical to clinical and contains 12 high-quality video lectures on topics agreed as essential by NIDA, NIAAA, SAMHSA, ASAM and AMERSA. The lectures are 25 – 40 minutes each, delivered by experts in the field, and also include interactive content. The lectures can be used as a set in a full elective course; and/or individually as part of other existing courses during any year of medical school.

Because medical education also involves case presentations, the course includes three "virtual cases" capturing common substance use related conditions that simultaneously illustrate important concepts in pathology, physiology, pharmacology and clinical care while also illustrating important aspects of the diagnosis, treatment and management of substance use disorders.

The course and virtual cases are supplemented with preparation for course instructors through a one-week, clinical immersion education experience at the Betty Ford Center.

Conclusions: This course was developed with guidance from medical school deans and key faculty; addiction experts, government agencies, and medical/scientific associations. It will be made available through subscriptions to medical schools that will enable them to meet the demands for more education and training about substance use disorders.

Financial Support: Scaife Family Foundation, Individual Donors

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IDENTIFICATION AND EVALUATION OF INTERNET FORUM DISCUSSION AS A COMPONENT OF A POST MARKET-SURVEILLANCE STRATEGY FOR TOBACCO PRODUCTS.

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Aims: To identify relevant Internet forums and to evaluate the feasibility of utilizing discussion to understand perceptions, behaviors, and use patterns associated with new tobacco products (NTPs) as part of a new post-market surveillance program.

General consensus supports the concept that tobacco surveillance should incorporate multiple and diverse approaches to provide both quantitative and qualitative data in a timely manner, including Internet data sources. Evaluating Internet content, including discussion (i.e., posts) on forums, may be a sensitive method for understanding and evaluating users' perceptions and behaviors associated with the introduction and use of NTPs in the market. We describe the process by which we identified and assessed these data to determine their applicability for use in post-market surveillance. Forums related to tobacco, particularly e-cigarettes and snus, were systematically identified on the Internet and data collection was piloted. Informed by findings from semi-structured interviews with e-cigarette and snus users as well as iterative reviews of forum discussion, a qualitative codebook was developed to capture content communicated within posts related to use of traditional (e.g., tobacco cigarettes) and new (e.g., e-cigarettes and snus) tobacco products (including brand specification), perceptions (e.g., safety, health), and behaviors (e.g., switching, use patterns). Coding was conducted on a sample of posts to assess the feasibility of answering two questions qualitatively: (1) what are the use patterns for cigarette smokers who start using e-cigarettes and (2) what safety perceptions do individuals have regarding snus?

Conclusions: Posts from Internet forums can be systematically identified, collected, and qualitatively coded to address research questions related to tobacco use patterns, behaviors, and perceptions associated with product use.

Financial Support: Inflexxion, Inc., Altria Client Services Inc.

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VALIDATION OF THE SUBSTANCE USE BRIEF SCREEN IN PRIMARY CARE.

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Aims: Implementation of substance use screening in general medical settings is hindered by the lack of a brief yet precise and comprehensive screening tool that is compatible with clinical workflows. To address this need, we developed the Substance Use Brief Screen (SUBS); a 4-item screener for tobacco, alcohol, and drug use (illicit and prescription) that is self-administered and may be easily integrated with electronic health records.

Methods: Adult patients were recruited consecutively in the waiting area of an urban safety net primary care clinic. The SUBS was self-administered in English on touchscreen tablet computers. Reference standard measures of unhealthy substance use and substance use disorders were then administered, including self-reported measures and saliva drug tests. The SUBS was compared against the reference standards to determine its sensitivity, specificity, and area under the curve (AUC) for each substance class.

Results: Among the 390 participants, rates of past year use reported on the SUBS were 37% tobacco, 43% alcohol (4+ drinks/day), 20% illicit drugs, and 12% prescription drugs. Sensitivity and specificity of the SUBS for detecting past year *unhealthy use* were: tobacco 99% and 91% (AUC=.95); alcohol 94% and 68% (AUC=.81); drugs (illicit or prescription) 84% and 89% (AUC=.86). Sensitivity was lower for prescription drugs (57%) than for illicit drugs (78%). For detecting a *substance use disorder*, sensitivity and specificity were: tobacco 100% and 73% (AUC=.87); alcohol 93% and 64% (AUC=.79); drugs 85% and 82% (AUC=.84).

Conclusions: The SUBS accurately identified unhealthy tobacco, alcohol, and drug use in this primary care sample, and had high sensitivity but lower specificity for identifying substance use disorders. Individuals screening positive on the SUBS should receive further assessment. Our findings support use of the SUBS for substance use screening in primary care, but additional tools may be needed for prescription drugs.

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OSMOTIC-RELEASE METHYLPHENIDATE RANDOMIZED CONTROLLED TRIAL FOR ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDERS AND SUBSTANCE USE DISORDERS: A MISSING DATA SENSITIVITY ANALYSIS.

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Aims: To examine sensitivity to missing data procedures on treatment effects in a randomized controlled trial (RCT) of osmotic-release methylphenidate (OROS) for adolescents with co-occurring attention-deficit/hyperactivity disorder (ADHD) and substance use disorders (SUD).

Methods: Data came from a National Drug Abuse Treatment Clinical Trials Network study (N=303, Riggs et al. 2011), which evaluated the safety/efficacy of a 16-week RCT of OROS vs. placebo in adolescents (aged 13-18) with ADHD who were also receiving cognitive behavioral therapy for their SUD. The two primary outcomes were clinician-reported ADHD symptoms and self-reported past 28 days of substance use (SU). We fit a parallel growth model and assessed the effect sizes assuming missing at random (MAR) compared to two missing not at random (MNAR) models; Diggle-Kenward (DK) selection model and Wu-Carroll (WC) selection model.

Results: Our MAR model found no significant treatment effect on ADHD or SU, and the effect sizes were small for both ADHD and SU (d=0.16, 0.10, respectively). The MNAR DK model also produced non-significant treatment effects with similar effect sizes of ADHD (d=0.03) and SU (d=0.11). The MNAR WC model evidenced a significant effect of OROS relative to placebo on SU, and the effect sizes for both ADHD (d=2.11) and SU (d=1.09) were larger than reported in the other models.

Conclusions: While the MAR model and one MNAR model found similarly sized effects as the original RCT, the second MNAR model produced different results for both of the outcomes. This sensitivity analysis highlights an important need for future RCTs of co-morbid mental illness and SUDs to carefully evaluate the missing data assumptions made when assessing treatment effects.

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GLUCOCORTICOID-ENDOCANNABINOID INTERACTIONS IN THE PRELIMBIC CORTEX MEDIATE STRESS-POTENTIATED REINSTATEMENT OF COCAINE SEEKING.

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Aims: Under certain self-administration conditions, stress alone does not reinstate cocaine seeking. However, stress, such as electric footshock stress (EFS), can potentiate reinstatement when paired with a low dose of cocaine and this effect is corticosterone-dependent. Corticosterone (CORT) may exert its action through an interaction with the endocannbinoid (eCB) system as cannabinoid receptor 1 (CB1R) dependent effects on neurotransmission in the medial prefrontal cortex, a region that is critical for reinstatement, are dependent upon glucocorticoids. The current study examined the involvement of the CB1R, specifically in the prelimbic cortex (PLC), in stress-potentiated reinstatement of cocaine seeking.

Methods: Male Sprague-Dawley rats self-administered cocaine (0.5 mg/kg/inf) 14 x 2 hrs/day on a FR4 schedule. Rats underwent extinction followed by stress-potentiated reinstatement tests, EFS + low dose cocaine (2.5 mg/kg i.p.). To test the involvement of the PLC, rats were given an intra-PLC infusion of CORT (0.05 μg/.03 μL) instead of EFS 15 min prior to the low dose cocaine injection. To test the involvement of CB1R, rats were given a systemic injection of the CB1R antagonist, AM251 (0, 1, 3 mg/kg i.p.) 30 min prior or an intra-PLC infusion of AM251 (0, 0.3 μg/0.3μL) 15 min prior to EFS.

Results: EFS paired with a low dose of cocaine induced reinstatement of cocaine seeking whereas either given alone did not. This effect was mimicked when intra-PLC infusions of CORT were paired with low dose cocaine suggesting CORT actions in the PLC mediate stress-potentiated reinstatement. Systemic AM251 blocked stress-potentiated reinstatement. Furthermore, preliminary data suggests that intra-PLC AM251 also blocks stress-potentiated reinstatement.

Conclusions: Taken together, these data suggest that corticosterone actions in the PLC, likely through an interaction with the eCB system, mediate stress-potentiated reinstatement.

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TRANSITIONS IN POLYDRUG USE AMONG HEROIN AND METHAMPHETAMINE INJECTORS IN TIJUANA, MEXICO.

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Aims: Although most people who inject drugs (PWID) in Tijuana primarily inject heroin, use of methamphetamine and co-injection of meth and heroin is also common. We examined patterns and transitions in polydrug use to inform prevention and treatment of drug use and its health and social consequences.
Methods: PWID residing in Tijuana aged ≥ 18 years were recruited through respondent driven sampling from 2006-2007. Participants underwent interviewer-administered surveys and testing for HIV, TB, and syphilis at baseline (n=1056) and 12 month follow-up (n=692). Latent class analysis was first conducted to assign individuals to classes on a probabilistic basis, using 4 indicators of past 6 month polydrug use: 1) heroin injecting, 2) meth injecting, 3) meth non-injecting, and 4) co-injection of heroin and meth. Latent transition analysis was then conducted to assess transition probabilities between polydrug use latent classes from baseline to 12 month follow-up.
Results: Latent class analyses indicated 3 classes at baseline (a heroin and meth use class, a meth use class, and heroin use class) and 4 classes at 12 months (a heroin and meth use class, meth use class, a heroin use class, and a heroin and meth co-injection class). Of those in the heroin and meth class at baseline, 25% stayed in this class, 48% transitioned to the heroin and meth co-injection class, and 27% transitioned to the heroin injecting class at 12 months. Of those in the heroin use class at baseline, 83% stayed in this class and 13% transitioned to the heroin and meth co-injection class at 12 months. Of those in the small but stable meth use class at baseline, 85% stayed in this class at 12 months.
Conclusions: Transitions between qualitative subtypes of polydrug use among injecting drug users were identified based on heroin and meth injection, non-injection, and co-injection use patterns. The emergence of a new class at 12 months defined by heroin and meth co-injection could signal a growing risk for overdose and other negative consequences of polydrug use.
Financial Support: T32 DA023356

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ADDICTION AND BARRIERS TO TREATMENT IN A SAMPLE OF COMMUNITY-RECRUITED METHAMPHETAMINE USERS IN A SOUTH AFRICAN TOWNSHIP.

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Aims: South Africa has experienced a dramatic increase in methamphetamine ("meth") use over the past decade. While evidence-based treatments are available free of charge, uptake is low. The purpose of this study was to describe substance abuse histories, addiction symptoms, and treatment utilization in a community-recruited sample of meth users.
Methods: Using respondent driven sampling, 360 active meth users were enrolled May-November 2013. Recent meth use was verified using a urine drug screen. Trained fieldworkers administered the Addiction Severity Index and the Composite International Diagnostic Interview. Participants also completed measures of behavioral risk using audio computer assisted self-interview.
Results: The sample included 196 men and 157 women. The majority was Coloured (73%) and ≤35 years old (83%) and did not graduate from high school (88%). Participants had been using meth regularly for <1-20 years (M=7.2, SD=4.3). On average, they used meth on 23.6 (SD=8.9) days out of the last 30, and 60% reported daily use. Concurrent use of marijuana (77%) and Mandrax (64%) were common. The majority (90%) met ICD-10 criteria for dependence. Only 11% of participants had ever sought treatment for meth use, but 90% reported that they wanted treatment. The primary motivators for treatment were: "sake of my children" and wanting a "better life" or to be "drug free". Among participants who had not sought treatment, many indicated a lack of knowledge about addiction and treatment options. We are currently analyzing in-depth interviews with 30 participants that will provide additional insight into perceptions of addiction and treatment.
Conclusions: Respondent driven sampling was an effective strategy for reaching a highly addicted group of meth users in need of treatment. Strategies are urgently needed to effectively link meth users to available treatments in the community.
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ATTITUDES, BELIEFS, AND BARRIERS TO ADOPTING AN AUTOMATED NALOXONE DELIVERY SYSTEM TO OVERCOME OPIOID OVERDOSE: INTERVIEWS OF OPIOID INJECTORS AND PHYSICIANS.

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Aims: Overdose (OD) is a common in illicit opiate users as well as patients treated with opioids for pain management – every year ~2000 heroin and 13,000 prescription opioid OD deaths occur in the US. We studied the attitudes, strengths, and barriers to adoption of an Automated Naloxone Delivery System (ANDS), a device designed to sense impending opioid OD and automatically deliver intranasal naloxone, in illicit opiate injectors and physicians who prescribe opiates.
Methods: In this pre Phase I study, we designed the physiological monitoring and prediction algorithm for triggering naloxone administration, and developed a prototype of the ANDS. Nine heroin injectors and nine physicians who regularly administer opioids were interviewed to identify the potential use and usability of the ANDS. Interviewees were encouraged to wear an ANDS prototype and attach sensors during the interview. Subjects rated the usability of the ANDS components, and overall ratings for acceptability, and ease and likelihood of use.
Results: Both physicians and opiate injectors found the ANDS simple and easy to use and rated benefit greater than burdens. Physicians were interested in the ANDS and suggested several in and out of hospital locations and situations where the device could be useful. They provided feedback on clinical use, and suggested components and designs that would make adoption into practice more likely Opiate injectors were interested in and would use a device that can automatically detect and save a life in the event of an OD.
Conclusions: This feasibility study resulted in a detailed design for a device to detect opioid OD reliably, administer naloxone consistently, and automate the process of OD reversal for users (who are often alone) and for patients who are receiving opiate therapy but are not continuously monitored.
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THE ROLE OF NOCICEPTIN IN RESPONDING FOR PALATABLE REWARDS.

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Aims: Opioid peptides are implicated in processes related to reward and aversion; however, the how specific opioid peptides are involved remains unclear. Here, we aim to investigate the role nociceptin in behavioral responding for palatable and aversive tastants.
Methods: A microstructural licking analysis of the effects of intracerebroventricular administered nociceptin on total licks, total bouts of licking, and lengths of licking bouts was conducted. Additionally, we compared these licking behaviors in wildtype and nociceptin receptor (NOP) knockout mice, to identify the role of endogenous nociceptin in these processes. We hypothesize that NOP knockout mice will show lower levels of licking behavior under normal conditions and will be irresponsive to the appetite-stimulating effects of nociceptin administration.
Results: Repeated measures ANOVA analyses show that NOP knockout mice generally emit fewer licks than wildtype mice when given access to sucrose solution. Furthermore, results from post-hoc analyses show nociceptin administration increases total number of licking bouts in wildtype mice in both chow sated and hungry states, an effect that was absent in NOP knockout mice. Similar effects were seen for the non-caloric sweetener sucralose, but to a lesser degree. Hunger tended to increase total bouts of licking for sucrose in all mice, but also increased mean bout length in NOP knockout mice only. Finally, adulterating sucrose solution with the bitter aversive tastant quinine produced similarly suppressive effects in both wildtype and NOP receptor knockout mice.
Conclusions: Together, these results support our hypothesis, suggesting that endogenous nociceptin contributes to the positive incentive properties of palatable tastants. Further understanding of the contributions of opioid neurotransmission to hedonic processing may aid in developing appropriate treatment strategies for pathologies characterized by aberrant reward seeking and taking behaviors.
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TIME TO FIRST CIGARETTE: A POTENTIAL CLINICAL SCREENING TOOL FOR NICOTINE DEPENDENCE AND CANCER RISK.

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Aims: To provide a synthesis of the accumulating literature on the relations of the time to the first cigarette (TTFC) of the day with nicotine dependence and cancer risk, identify gaps, and inform future clinical and epidemiological research of potential uses of TTFC.
Methods: A comprehensive narrative review of the literature was conducted using PubMed, Google Scholar, and Web of Science ISI databases. Twenty articles were identified which examined the relation between TTFC and dependence outcomes, and eight articles were identified which examined the relation between TTFC and cancer risk.
Results: Across all reviewed studies, earlier TTFC was associated with greater cancer risk, greater likelihood of cessation failure and relapse, and higher levels of nicotine, tobacco, and carcinogen exposure. Several of these relationships were found among both adult and teen smokers, and remained even after accounting for smoking behaviors such as cigarettes per day.
Conclusions: Earlier TTFC is a key indicator of greater nicotine dependence and greater risk for tobacco-related cancers. Knowledge of a smoker's TTFC may allow clinicians to accurately inform patients of health consequences of smoking and assign greater resources to smokers during cessation attempts. Smokers themselves may be able to use TTFC to self-select cessation aids, as well as accurately assess their unique smoking-related health risks. TTFC may be a better item than cigarettes per day for accurately quantifying risk in epidemiologic studies.
Financial Support: Ms. Mercincavage was supported by training grants UL1 TR000127/TL1 TR000125 from the National Center for Advancing Translational Sciences (NCATS).

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CAFFEINE INCREASES THE REINFORCING EFFECTS OF ALCOHOL IN SOME SOCIAL DRINKERS.

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Aims: Co-consumption of caffeine and alcohol has been associated with increases in reckless behavior and alcohol-related injury. One possible explanation for this relationship is that caffeine increases alcohol consumption by enhancing the reinforcing effects of alcohol-containing beverages, which, in turn, may lead to increases in alcohol-related problems. It is also possible that caffeine interferes with the discriminability of alcohol-related behavioral impairment while having no effect (or less of an effect) on behavioral impairment. Therefore, individuals consuming alcohol mixed with caffeine may engage in risky behaviors because they judge that they are less impaired than they actually are. The aims of the current study were to test these two hypotheses.
Methods: A double-blind, placebo-controlled, repeated-measures laboratory investigation, compared subjective, motor/cognitive, and reinforcing effects of beverages containing alcohol (78 g/l) + caffeine (333 mg/l) versus beverages containing alcohol (78 g/l) + placebo (i.e., quinine; 12.2 mg/l) in 19 social drinkers with histories of regular caffeine consumption. During 6 ad libitum consumption sessions, participants consumed alcohol + caffeine on 3 session days and alcohol + placebo on 3 session days. On a subsequent, final session day, participants chose which beverage they would consume during that session.
Results: More participants chose alcohol + caffeine (n = 13) than alcohol + placebo (n = 6). Data from the first 6 sessions showed that, compared to placebo choosers, caffeine choosers consumed more alcohol + caffeine relative to alcohol + placebo, and they reported more positive subjective effects when consuming alcohol + caffeine relative to alcohol + placebo. Across all participants, following consumption of alcohol + caffeine, performance on a reaction time task was less impaired than it was following consumption of alcohol + placebo.
Conclusions: The results suggest that, for some consumers, alcohol mixed with caffeine is more reinforcing than alcohol alone.
Financial Support: This research was supported by NIH grants R01DA03890 and T32DA007209.

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MANAGING SUBSTANCE USE TREATMENT IN PRIVATE U.S. HEALTH PLANS.

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Aims: Health strategies to manage utilization of substance use disorder (SUD) treatment may impact treatment access and delivery. This study provides national estimates of health plans' management strategies.
Methods: Data are from a nationally representative survey of private U.S. health plans in 2010 (N= 351 plans, with 939 products; 89% response rate). For each of the three most commonly purchased insurance products, respondents reported on availability of information to enrollees seeking treatment, prior and continuing authorization requirements, medical necessity criteria, and waiting time standards. Results are weighted to provide national estimates.
Results: In online provider directories, nearly 90% of health plan products include providers' specialized expertise, but only 25% include provider performance on satisfaction or quality measures. Only 5% of products required prior authorization for outpatient SUD care. However, 76% required authorization to continue outpatient treatment. Over 90% of products required prior and continuing authorization for higher levels of care. ASAM placement and self-developed criteria were the most common criteria used for prior authorization. Medical necessity criteria were made available to providers and enrollees upon request and denial of services by over 90% of products. Almost all products had formal standards to limit waiting time for routine and urgent treatment, but one-third did not have such standards for detoxification services. Patient surveys and complaint analysis were common methods to monitor wait time.
Conclusions: Findings indicate plans use a range of techniques to manage care, but prior authorization, a long-standing technique, was seldom required for outpatient SUD care. Understanding utilization management is of particular interest in the wake of federal parity legislation that curtails the use of more stringent management for behavioral health than is imposed for other medical care.
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CHARACTERISTICS AND QUALITY OF LIFE OF OPIOID-DEPENDENT PREGNANT WOMEN IN AUSTRIA.

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Aims: This study investigated pregnant opioid-dependent women undergoing maintenance therapy, applying a multidisciplinary, case-management approach at the Addiction Clinic of the Medical University of Vienna, Austria. It aimed at characterizing the patients' basic demographic and clinical parameters and evaluating their overall quality of life (QoL) pre- and postpartum.
Methods: 390 women were treated between 1994 and 2009 with buprenorphine (n=77), methadone (n=184), or slow-release oral morphine (SROM) (n=129) on an outpatient basis throughout their pregnancy and postpartum period. All patients were subject to standardized pre- and postpartum medical and psychiatric assessments, including QoL assessments using a German adaptation of the Lancashire QoL Profile, and regular supervised urine toxicologies.
Results: No medication group differences were revealed regarding basic demographic or clinical data. Mean maintenance doses (SD) at time of delivery were: 64mg (36mg) methadone, 10mg (6mg) buprenorphine, 455mg (207mg) SROM. However, buprenorphine-medicated women showed significantly less concomitant benzodiazepine consumption than methadone- or SROM-maintained women ($p=0.005$), and significantly less concomitant opioid consumption than methadone-maintained women ($p=0.033$) during the last trimester. Overall QoL was good pre- and postpartum in all measured domains except "finances" and "prospect of staying in the same housing situation", and no differences were observed in QoL among the 3 medication groups ($p=0.177$). QoL improved significantly after delivery in most of the domains ($p<0.001$).
Conclusions: Although opioid-dependent pregnant women face high-risk pregnancies and show variability in addiction severity, they report good QoL independent of the medication administered. These results show that individually tailored treatment interventions are effective for this patient population and suggest a QoL improvement after delivery.
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GENDER DIFFERENCES IN SMOKING AND TREATMENT OUTCOME AMONG OPIOID-MAINTAINED SMOKERS.

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Aims: Prior studies have suggested that gender differences may exist in the general population of smokers, with males often presenting with greater nicotine dependence yet showing better treatment response than females. Less is known about possible gender differences in hard-core subgroups of smokers, such as substance abusers. The present secondary analysis examined this question in opioid-maintained smokers receiving a behavioral intervention to promote smoking abstinence.
Methods: Opioid-maintained smokers received a brief intervention aimed at establishing initial smoking abstinence and included daily visits, biochemical verification of smoking status via breath carbon monoxide and urinary cotinine, and financial incentives contingent upon abstinence. Participants were dichotomized based on gender, and differences in intake characteristics and treatment outcomes were analyzed.
Results: Participants (52 males, 68 females) were 33 yrs old and had 12 yrs education. Males smoked more cigarettes per day (20 vs. 17 cigs/day; p=.03), had higher urinary cotinine levels (1537 vs. 1240 ng/ml; p=.01) and scored higher on the Fagerstrom Test for Nicotine Dependence (5.7 vs. 4.8; p=.02) than females, respectively. Males also showed less intention to smoke on the Questionnaire on Smoking Urges (35.3 vs. 45.1; p=.003). With regard to treatment response, males achieved significantly greater smoking abstinence, submitting 61% smoking-negative samples vs. 54% in females (p=.004). In addition to these primary outcomes, we will also examine gender differences in nicotine withdrawal and craving for inclusion in this June 2014 presentation.
Conclusions: Consistent with prior studies in the general smoker population, opioid-maintained males exhibited greater nicotine dependence yet responded better to an intervention offering abstinence-contingent financial incentives. These data suggest that gender differences may also exist in substance abusers and extend these findings to opioid-dependent smokers receiving an empirically-supported behavioral intervention.
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LONGITUDINAL GENDER DIFFERENCES IN HIV AND CRIMINAL JUSTICE OUTCOMES.

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Aims: Inform gender-specific HIV interventions among criminal justice (CJ) populations by evaluating gender differences in HIV and CJ outcomes.
Methods: Longitudinal CJ, pharmacy, and laboratory databases were linked in a retrospective cohort of HIV+ prisoners on ART. Gender differences were quantified by type of criminal offenses, incarceration periods, and HIV treatment outcomes. Logistic regression models identified correlates of viral suppression (VS; HIV-1 RNA<400) among women with p<0.05 being statistically significant (*).
Results: Among 1089 HIV+ prisoners on ART, compared to 866 men (1620 incarceration periods), the 223 women (461 incarceration periods) were more likely to be younger (mean 40.2 v 43.3 years*), white (30.9% vs. 17.2%*), have medical insurance (51.6% v 9.1%*), have shorter incarceration periods (mean 181.0 v 327.2 days*) and commit more non-violent misdemeanors (58.0% v 46.0%*) and public order offenses (44.1% v 32.1%*). During incarceration periods, women were more likely than men to receive antidepressants (69.1% v 41.3%*), medication-assisted therapy for opioid dependence (17.5% v 10.4%*) and achieve VS before release (80.0% v 68.7%*). Upon CJ entry, one-third of women had VS, correlating with older age (aOR 1.08, 95%CI 1.02-1.14), receiving treatment for other comorbidities, and prescribed single fixed-dose ART combinations (aOR 2.28, 95% CI 1.02-5.13).
Conclusions: In the largest contemporary cohort of HIV+ prisoners on ART, women's incarceration and HIV treatment outcomes differed in critical and dynamic ways from men's, providing insight into addressing gender-related health disparities. The higher prevalence of non-violent offenses and increased comorbidities of women, especially treatable substance use disorders, supports alternatives to incarceration strategies. Interventions for HIV+ CJ populations should be gender-specific to effectively align health and justice goals.
Financial Support: Funding was through a Bristol Myers-Squibb Virology Fellows Award (JM) and career development grants from NIDA (K23 DA033858 JM, F31 DA035709 JC, K24 DA017072 FA). The funding sources played no role in study design, data collection, analysis, or interpretation.

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NOVEL GENETIC VARIANT ASSOCIATED WITH SUBSTANCE USE IN TWO INDEPENDENT POPULATIONS.

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Aims: Risky alcohol, nicotine, and marijuana use are the most common and costly public health problems in the United States. Family, twin and adoption studies have shown that frequency of alcohol, nicotine, and cannabis consumption each have a considerable genetic component, with heritability estimates in the range of 50%. In this study, we report results from a genome-wide association study (GWAS) of frequency of alcohol, nicotine, and marijuana consumption.
Methods: Number of alcoholic drinks consumed, number of cigarettes smoked, and marijuana consumed, per using day was retrospectively reported among a large population of 778 individuals of African ancestry from Detroit, Michigan, genotyped on the Illumina HumanOmniExpress Beadchip.
Results: GWAS analyses implicated four genome-wide significant effects; one of which was successfully replicated in an independent sample. SNP rs11766060 (p = 6.83× 10−8) located downstream of Even-Skipped Homeobox (EVX1) at 7q15. This finding was successfully replicated (p-value<0.01) in a population based sample of ~2000 individuals of African ancestry from Grady Memorial Hospital located in Atlanta, Georgia,
Conclusions: In conclusion, we identified and replicated a novel genetic variant, associated with frequency of substance use in two independent populations of African ancestry. These findings can improve the understanding about the etiology of substance use and related disorders.
Financial Support: NIMH

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NAVIGATING THE WORLD OF ADOLESCENT SUBSTANCE ABUSE TREATMENT THROUGH A WEB-BASED CONSUMER GUIDE.

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Aims: Consumers increasingly access the internet to obtain health related information and quality ratings of various medical providers, and "report cards" are increasingly common. It is disconcerting that the adolescent specialty substance abuse treatment (SAT) system is virtually absent from online review websites. An online guide that illustrates quality features of adolescent SAT is needed for parents seeking help for their children and other interested parties (e.g., referral sources, purchasers of treatment, adolescents themselves). Thus, we developed an online Consumer Guide to Adolescent SAT.
Methods: While quality problems in SAT have generated broad concern, there is no widely recognized process to rate the quality of SAT programs in a clinically comprehensive manner. There are however guidelines and models to assess quality. Using scientific evidence, expert review, and stakeholder input, a multistep research and development process was employed: reviewed the scientific literature, created a program interview and audit procedure to 'score' the programs, vetted this with experts, tested the program quality evaluation in community SAT clinics, and vetted the website itself with user groups (e.g., parents, physicians, judges).
Results: A transportable protocol now exists for implementation within municipalities or networks of providers to obtain a science-based comparative review of SAT programs. The website includes: user-friendly educational material on understanding the nature of SAT quality; a navigator function that asks core questions about a youth's potential service needs and identifies programs by location, type, and quality profile; and resources for additional support.
Conclusions: This protocol and the resulting Consumer Guide serves two critical purposes: inform and direct an individual consumer's purchase; and improve the service marketplace as informed consumers are essential to improving availability, quality and costs of services, particularly in healthcare.
Financial Support: P50 DA027841

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TRAJECTORIES OF NEIGHBORHOOD DISORDER, ALCOHOL INITIATION, AND ALCOHOL USE AMONG URBAN ADOLESCENTS.

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Aims: Initiation of alcohol, tobacco, and other drugs (ATOD) use closely follows opportunities to use ATOD. The transition from opportunity to use to initial use also is influenced by the age of the individual during initial opportunity; as the age at first opportunity to use increases the time from opportunity to initial use also increases. Given this prior research, it would be important to identify strategies to prevent early opportunities to use ATOD. This study aims to understand the impact of neighborhood disorder on opportunities to use alcohol and how neighborhood environment influences the transition from opportunity to use to initial use.
Methods: Data were obtained from the Baltimore Prevention Project, a longitudinal study of 678 predominately African American young adults who have been assessed longitudinally from first grade into young adulthood. Perceived neighborhood environment was measured using four items for the Neighborhood Environment Scale (NES) during 6th-9th grade (e.g. Every few weeks, some adult gets beat-up or mugged in my neighborhood). Growth mixture modeling (GMM) was used to the association between neighborhood trajectories, age of alcohol initiation, and age of first alcohol use.
Results: GMM produced a two-class model of neighborhood environment, high neighborhood disorder (76.8%) and low neighborhood disorder (24.2%). There was a marginally significant relationship between neighborhood trajectory and opportunities to use alcohol ($p = 0.067$). Additional models will examine how neighborhood environment effects the progression from opportunity to use alcohol to initiation of alcohol use.
Conclusions: This study found a trend between neighborhood environment trajectory and age of alcohol initiation and age of first alcohol use. These results suggest that preventing children's early exposure to deleterious neighborhood and/or providing children with strategies to "cope" with deleterious environments may reduce early exposure to and eventual use of alcohol.
Financial Support: NIAAA R01AA015196; CDC 5U01CE00195403

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MONKEY GENOMES: A PARADIGM SHIFT FOR ADVANCING PRECLINICAL RESEARCH AND MEDICATIONS DEVELOPMENT FOR ADDICTIONS.

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Aims: Monkeys are similar to humans and are essential models for addiction research, but their utilization is complicated by unidentified genetic variation. Candidate gene studies in rhesus monkeys have repeatedly demonstrated a striking parallelism, in both function and phenotypic association, with homologous human variants implicated in addiction. A hallmark example is the parallel functional and behavioral effects of mu-opioid receptor gene (OPRM1) variants on alcohol drinking behavior and pharmacogenomic sensitivity to naltrexone observed in rhesus monkeys and humans (DAD 109:252). Other examples will be reviewed. Here, we advance a paradigm shift in the way monkeys are utilized in addiction research. Now, new technologies can reveal genomic and epigenetic variation that underlies individual phenotypes, facilitating a transition from arbitrary to deliberate assignment of subjects into studies. Already the cost of a monkey's genome (~$1k) is dwarfed by its purchase (~$10k) and husbandry costs (~$4k/year). Inevitably, complete genomic datasets will soon exist for each monkey used in research. Although bioinformatics tools for analyzing large data sets exist, maximizing the biological relevance from genomic data requires systematic phenotyping of monkeys prior to allocation. A systematic strategy would allow for unique opportunities to assign functional meaning to genetic and epigenetic variation. A standard operating procedure for phenotyping will be discussed.
Conclusions: Environmental factors alter genetic influences on addiction-related phenotypes. Human studies are inherently confounded by variability of environmental histories, but monkeys have controlled and documented environmental histories. Further, studies can be longitudinal, semi-invasive and fully compliant. We coin the term "Translational Phenomics" to describe a priori genotype/phenotype assessments and the directed allocation of monkeys. This approach results in higher translational and clinical relevancy and an ability to bridge the gap between clinical and basic addiction research.
Financial Support: DA025697 (GMM), OD011103 (NEPRC), AA019688 (EJV)

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THE LONG-TERM IMPACT OF POST TRAUMATIC STRESS DISORDER ON RECOVERY FROM HEROIN DEPENDENCE.

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Aims: Post traumatic stress disorder (PTSD) is highly prevalent among individuals with heroin dependence. Although a number of studies have examined the impact of PTSD on treatment outcomes for heroin dependence in the short-term, none have investigated the impact of this disorder on long-term recovery. Using data collected as part of the Australian Treatment Outcome Study, the present paper aims to examine the impact of PTSD on heroin use over 10-11 years.
Methods: 615 people with heroin dependence were recruited to the study in 2001-2002, and more than 68% of the sample were re-interviewed in 2011-2013. DSM-IV diagnoses PTSD were obtained at study entry using the Composite International Diagnostic Interview version 2.1.
Results: At baseline, approximately 40% of the sample were diagnosed with lifetime PTSD and 30% were experiencing current symptoms. There were no significant differences between those with and without PTSD in terms of heroin or other substance use at the 10-11 year follow-up. Close to one-half were in treatment for their heroin dependence, approximately 25% were still using heroin, and 15% met criteria for a diagnosis of dependence. However, at the 10-11 year follow-up, those who met criteria for PTSD at baseline were significantly less likely to be employed, more likely to meet criteria for current major depression, and more likely to have attempted suicide over the follow-up period.
Conclusions: Consistent with research examining the short-term impact of PTSD on treatment outcomes for heroin dependence, the present study found that comorbid PTSD has a long-term impact on occupational functioning and mental health of individuals with heroin dependence. These findings highlight the importance of addressing underlying comorbid presentations among this group.
Financial Support: The Australian Treatment Outcome study was funded by the Australian National Health and Medical Research Council and the Australian Government Department of Health and Ageing.

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THE EFFECTS OF INTRANASAL OXYTOCIN ON SOCIAL COGNITION, IMPLICIT PREFERENCES AND CRAVING IN ALCOHOLICS.

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Aims: The ability to develop and maintain healthy interpersonal relationships is an important prognostic factor for successful treatment of alcohol and substance use disorders. Despite this finding, effective pro-social pharmacological treatments are not currently available. The neuropeptide oxytocin plays an important role in social behavior and attachment in animals and humans, increasing trust behavior and improving social cognition. Here we test the efficacy of oxytocin in promoting social behavior at the expense of drug use-related behavior in alcohol abusing individuals.
Methods: In a randomized, within-subject, cross-over study, oxytocin and placebo were administered intranasally to 32 alcohol abusing subjects in a human laboratory setting to examine whether intranasal oxytocin administration reduces social cognitive deficits, reduces craving for alcohol, reduces appetitive approach or cue reactivity to alcohol, or shifts implicit preferences from drug-related stimuli to social stimuli.
Results: Although our alcohol abusing population has basal impairment in the recognition of sarcasm compared to normative data, we find no significant improvement in recognition of sarcasm ($p = .60$, $n = 32$), nor in recognition of facial emotions following oxytocin administration ($p = .61$, $n = 31$). However, in subjects initially showing appetitive approach to alcohol, there is a significant attenuation in this approach following oxytocin administration ($p = .006$, $n = 18$). Additionally, there is a trend towards a negative correlation between the effects of oxytocin on appetitive approach and AUDIT score ($p = .09$) and LOC score ($p = .03$) and a trend towards greater craving for alcohol following oxytocin administration ($p = .06$, $n = 32$).
Conclusions: These data suggest that oxytocin administration can attenuate appetitive approach to alcohol-associated cues. This research offers a first step towards identifying oxytocin as an adjunct treatment for alcohol and substance use disorders, though not perhaps by improving social cognition.
Financial Support: Wheeler Center for the Neurobiology of Addiction and DOD IMN.

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EXECUTIVE FUNCTIONING AND EMOTION DYSREGULATION IN ADHD AND NON-ADHD CIGARETTE SMOKERS.

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Aims: Adults with attention-deficit/hyperactivity disorder (ADHD) smoke in part to regulate ADHD symptoms. In addition, emotion dysregulation and executive functioning (EF) are also proposed to influence smoking. We aimed to (a) assess group differences in emotion dysregulation and EF between smokers with and without ADHD and (b) address the role of emotion dysregulation and EF when smokers reported on changes in their ADHD symptoms after smoking using ecological momentary assessment (EMA).
Methods: In study 1, smokers with (n=23, M age=33.04) and without (n=13, M age=29.92) ADHD completed measures of emotion dysregulation (Difficulties in Emotion Regulation Scale [DERS]) and EF (Deficits in Executive Functioning Scale [DEFS]). In study 2, 17 smokers with ADHD (M age=32.29) completed baseline measures of emotion dysregulation and EF, then provided EMA ratings of change in ADHD symptoms after smoking.
Results: In study 1, a series of ANCOVAs covarying nicotine dependence indicated that ADHD smokers yielded higher scores than non-ADHD smokers on the following emotion dysregulation facets: lack of emotion acceptance, goal-directed behavior when distressed, impulse control, effective emotion regulation strategies, and emotional clarity (p's <.01). They also reported greater EF problems (p <.001). In study 2, multi-level modeling analyses indicated that those higher in DERS Lack of Emotion Acceptance reported a greater reduction of hyperactive-impulsive (p=.02) and inattentive (p=.001) symptoms after smoking than lower scorers. Those higher in EF problems at baseline reported a greater reduction of inattentive symptoms (p=.02) after smoking.
Conclusions: EF difficulties and emotion dysregulation were elevated in adults with ADHD who smoke. Also, although adults with ADHD smoke to regulate ADHD symptoms, these effects are most pronounced for those lower in EF and emotion regulation.
Financial Support: This work was supported by the National Institute of Drug Abuse (R03 DA029694 to J.T.M. and K23 DA032577 to J.T.M., K24 DA02344 to S.H.K., and K24 DA016388 to J.C.B.).

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ADOLESCENT SBIRT IMPLEMENTATION IN AN URBAN FQHC: THE FIRST 6 MONTHS.

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Aims: To examine baseline provider attitudes and 6-month outcomes of an ongoing cluster randomized trial comparing the implementation of generalist vs. specialist-delivered adolescent SBIRT services in seven primary care sites of an urban federally qualified health center.
Methods: Prior to completing training in either the specialist or generalist models of adolescent SBIRT service delivery, health care staff and administrative personnel (n=92) across the 7 participating primary healthcare sites completed baseline surveys assessing acceptability and feasibility of providing SBIRT services. Following implementation of the models at each clinic, data were extracted monthly from the electronic medical record for the next 6 months to determine penetration of adolescent SBIRT services and adherence to the service delivery model.
Results: The perceived benefit of screening and providing brief interventions for adolescent substance use was high for all health personnel, including medical assistants, primary care providers (PCPs), and mental health, however uncertainly regarding patient truthfulness about substance use was also common. Time constraints were perceived to be the greatest barrier to providing brief interventions. In the first 6 months of implementation the screening rates across both conditions increased from approximately 25% in month 1, to 70% in month 6. Percentage of patient visits appropriately counseled to continue abstinence from alcohol and/or illicit drug use were comparable across conditions, however the provision of counseling to stop/reduce alcohol and/or illicit drug use was less consistently provided in the specialist than the generalist sites.
Conclusions: Perceived need and support for adolescent SBIRT services in this urban federally qualified health center was high. Screening rates increased substantially within the first 6 months of implementation and differences in service delivery patterns were starting to emerge.
Financial Support: NIDA 1 R01 DA034258 (S.G. Mitchell, PI)

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THE ROLE OF $GABA_A$ RECEPTORS ON ETHANOL-INDUCED TYPE 1 IP_3 RECEPTOR UP-REGULATION.

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Aims: Previous reports have revealed modification of pharmacological action of ethanol by $GABA_A$-Rs and our previous studies demonstrated that IP_3R-1 up-regulation in mouse brain with place preference induced by drugs of abuse. The present study attempted to clarify the role of $GABA_A$-Rs in IP_3R-1 up-regulation after long-term ethanol exposure using mouse cerebral cortical neurons.
Methods: On the 10th day of culture, the neurons were incubated with SCH23390 (a selective dopamine D_1 receptor antagonist), bicuculline (a selective $GABA_A$-R antagonist; 10 μM), and muscimol (a selective $GABA_A$-R agonist; 10 μM) 1 h before the exposure to ethanol (50 mM) and thereafter incubated with ethanol, bicuculline, and muscimol for 72 h to measure IP_3R-1 protein expression and for 6 h to examine IP_3R-1 mRNA level.
Results: Long-term exposure to ethanol induced IP_3R-1 protein up-regulation following increased expression of its mRNA. SCH23390 suppressed the ethanol-induced up-rgulation of IP_3R-1 protein and mRNA. Pre-treatment with muscimol significantly suppressed these ethanol-induced changes, which was significantly abolished by bicuculline.
Conclusions: The present results indicate that $GABA_A$-Rs negatively regulate the ethanol-induced up-regulation of IP_3R-1 protein expression via the suppression of gene transcription. Recent our report demonstrated stimulatory role of dopamine D_1 receptors in IP_3R-1 up-regulation. Furthermore, ethanol has stimulatory potential to release dopamine and to increase dopamine D_1 receptor expression in cortical neurons. Taken together with these data, the inhibition of ethanol-induced IP_3R-1 up-regulation by $GABA_A$-R activation may be due to direct inhibitory interaction of $GABA_A$-Rs with dopamine D_1 receptors or suppressive action of $GABA_A$-Rs on dopamine release by ethanol, though the exact mechanisms remain to be elucidated.
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FEMALE COCAINE USERS ARE AT EXCESS RISK OF BECOMING COCAINE DEPENDENT SOON AFTER ONSET OF COCAINE USE: ESTIMATES FOR THE UNITED STATES, 2002-2011.

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Aims: In this research project, we re-visit previously published estimates that suggested no male-female variation in risk of becoming cocaine dependent among newly incident cocaine users, seeking to learn about the possible changing epidemiology of cocaine use in more recent years. The main aim is to estimate the size of the male-female difference in the probability of making a rapid transition from first use of cocaine until the onset of cocaine dependence, if any difference exists.
Methods: The study estimates are based on the United States (US) National Surveys of Drug Use and Health conducted between 2002 and 2011, each with a nationally representative sample of non-institutionalized civilians age 12 years and older (n>50,000 each year). Weighted data with complex survey variance estimates yield year-specific 95% confidence intervals (CI) reported below, from which a sample size of 1684 newly incident users can be determined. A random effects meta-analysis approach is used to summarize estimates from 2002-3, 2004-5, 2006-7, 2008-9, and 2010-11.
Results: Via this meta-analytic approach, we discovered emergence of a statistically robust male-female difference, with excess risk of cocaine dependence seen for newly incident female cocaine users (9% and 95% CI = 6.30%, 11.04%) vs. a corresponding incidence estimate of 5% for males (95% CI = 3.56%, 6.28%) at $p < 0.05$.
Conclusions: Whereas underlying sex-associated neurobiological and neuropsychopharmacological mechanisms can be discussed in relation to this facet of cocaine epidemiology, it also is possible that the changing epidemiology of cocaine use in the US includes different non-random cocaine use selection processes than were present in earlier stages of the country's most recent cocaine epidemic. The possibility of recent differential male selection into newly incident methamphetamine use requires exploration.
Financial Support: Supported by NIDA T32DA021129 (AMM); K05DA015799 (JCA).

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CAN WE USE CUE-RELATED BRAIN RESPONSES TO PREDICT WHICH COCAINE PATIENTS WILL TAKE MORE RISKS?

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Aims: Some addicted individuals take high risks in the pursuit of drug reward, despite potentially severe negative consequences (e.g., incarceration, injury, STI/HIV infection through unprotected sex, even loss of life). We hypothesized that riskier individuals are **either** more sensitive to the motivational "pull" of reward cues, **or** less able to modulate this "pull", or **both**. To test this hypothesis, we performed a correlation between the brain response to drug reward cues and risk-taking scores on the Balloon Analogue Risk Task (BART). We predicted that higher risk taking would be *positively* correlated with cocaine cue-triggered activity in nodes of the mesolimbic reward ("GO!") circuitry, but *inversely* correlated with activity in prefrontal modulatory ("STOP!") regions associated with the evaluation and regulation of reward.
Methods: Cocaine-addicted inpatients (n=19, ongoing) were scanned with event-related BOLD fMRI during exposure to brief (500 msec) evocative (cocaine, sexual, aversive) vs. neutral cues. After scanning, the participants' risk-taking behavior was assessed using the BART. BART scores (average adjusted pumps) were then used as regressors in a pre-planned cocaine-neutral cue contrast.
Results: As predicted, BART scores correlated *positively* with cue-triggered activation in several reward-relevant nodes, caudal OFC, l. amygdala, l. pallidum, and l. insula ($p<0.05$, uncorrected). Risk-taking behavior correlated *negatively* with activation in two modulatory regions, lateral OFC and dorsal ACC ($p<0.05$, uncorrected).
Conclusions: This is the first report, to our knowledge, that the brain response to drug reward cues can be used to predict risk-taking in addicted individuals. Medications targeting cue-related brain responses may have a dual public health benefit: 1) reducing cue-triggered relapse, and 2) reducing the willingness of addicted individuals to take health-threatening risks for drug reward.
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INITIAL ABSTINENCE STATUS AND CONTINGENCY MANAGEMENT TREATMENT OUTCOMES: DOES RACE MATTER?

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Aims: This study evaluated the efficacy of Contingency Management (CM) among African American and White cocaine users.
Methods: A secondary analysis evaluated effects of race, treatment condition, and baseline cocaine urine sample results on treatment outcomes of African American (n = 444) and White (n = 403) cocaine abusers participating in one of six randomized clinical trials comparing CM to standard care.
Results: General Linear Modeling analyses revealed a significant 3-way interaction between race, baseline cocaine urine toxicology results and treatment group on the percentage of negative samples submitted during treatment ($F [1, 835] = 5.46$, $p < .05$) and weeks retained in treatment ($F [1, 835] = 5.32$, $p < .05$), but this interaction effect was not significant for longest duration of abstinence achieved during treatment, $F (1, 835) = 2.04$, $p = .15$. Specifically, African American and White adults who initiated treatment with a cocaine-negative urine sample remained in treatment for similar durations and submitted a comparable proportion of negative samples during treatment regardless of treatment type. Whites who began treatment with a cocaine positive sample remained in treatment longer and submitted a higher proportion of negative samples when assigned to CM than standard care. African Americans who initiated treatment with a cocaine positive sample, however, did not remain in treatment longer with CM compared with standard care, and gains in terms of drug use outcomes were muted in nature relative to Whites. This interaction effect persisted through the 9-month follow-up period.
Conclusions: CM is not equally effective in reducing drug use among all subgroups, specifically African American patients who are using cocaine upon treatment entry. African Americans are in need of effective treatment that will not only prevent relapse but also initiate cocaine abstinence.
Financial Support: This research was supported by NIH grants P30-DA023918, P50-DA09241, R01-DA016855, R01-DA027615, and R01-HD075630.

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DELAY DISCOUNTING IN POLYSUBSTANCE DEPENDENCE.

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Aims: Substance dependence is a major public health concern in the United States. Moreover, most individuals with substance dependence are engaged in poly substance abuse with 75% of individuals in treatment for alcohol and cocaine dependence also smoke cigarettes. The effects of concurrent substance dependencies are pertinent to treatment planning, treatment efficacy and understanding the neurobiological underpinnings of addiction. One measure of the impact of multiple drug dependencies is to examine the extent that such individuals discount future rewards. A prerequisite to targeted corrective interventions is an understanding of the differences between non-substance users, mono-substance users, and poly-substance users. We hypothesize that increased number of dependencies will correlate with steeper discounting of future rewards.
Methods: We compared 62 individuals with no substance dependencies, 143 individuals with nicotine dependence, 218 individuals with co-occurring nicotine and cocaine, alcohol or cocaine and alcohol dependence. Each participant completed a delay discounting task to measure the rate of discounting of future rewards.
Results: Individuals with co-occurring alcohol, cocaine, and nicotine dependence discounted future rewards significantly more than individuals who were tobacco dependent. Furthermore, individuals with no substance dependencies discounted future rewards significantly less than individuals with multiple substance dependencies.
Conclusions: These results provide evidence that poly-substance dependent individuals discount future rewards more than controls and mono-dependent cigarette smokers. These results support the importance of further study regarding the impact of co-occurring substance dependencies and how treatment for individuals with multiple dependencies may require different approaches than those with single dependencies.
Financial Support: NIDA (R01DA024080, R01DA030241), NIAAA Supplement (R01DA024080), and the VTCRI

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METHAMPHETAMINE DEPENDENCE, PSYCHIATRIC DISORDERS, AND TREATMENT OUTCOMES IN INDIVIDUALS TREATED WITH METHYLPHENIDATE.

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Aims: The aim of this study is to examine the prevalence of psychiatric disorders and the association between psychiatric disorders and treatment outcomes in a sample of MA-dependent study participants.
Methods: This secondary analysis utilizes data collected in randomized, double-blind, placebo-controlled study of 110 MA-dependent adults randomly assigned to pharmacotherapy with methylphenidate (MPH) or placebo for 10 weeks in combination with weekly cognitive behavioral therapy (CBT), followed by 4-weeks of single-blind placebo. To examine the relationship between psychiatric diagnoses and substance use outcomes, psychiatric diagnoses were assessed with the MINI at baseline, and MA use was assessed using the Treatment Effectiveness Score (TES) which calculates a score using urine drug screens (UDS) collected twice weekly.
Results: A total of 67.3% (N=74) of the sample met DSM-IV criteria for a psychiatric disorder; 30.3% (N=33) for Major Depressive Disorder, current; 10.1% (N=11) for a psychotic disorder, and 32.1% (N=35) for Antisocial Personality Disorder. The presence of a psychiatric disorder was associated with a significantly greater likelihood of amphetamine positive UDS at the end of the active medication phase (i.e. Weeks 9 & 10 [P=0.006]). Having a psychiatric disorder was also associated with increased CBT attendance in the placebo group (P=0.01) but was not associated with treatment retention in either group.
Conclusions: This study included a relatively high prevalence of psychiatric diagnoses among participants, similar to other treatment research. The presence of a psychiatric disorder was associated with MA use outcomes suggesting the need for attention to screening and treatment needs within dually diagnosed populations.
Financial Support: National Institute on Drug Abuse DA015084, medication supplied by Janssen Pharmaceuticals.

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CALL BEHAVIOR AND REPORTED DRUG USE WITHIN AN AUTOMATED TELEPHONE-BASED TREATMENT SYSTEM FOR METHADONE PATIENTS.

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Aims: Within a pilot randomized trial of the Recovery Line, an automated telephone-based treatment system for opioid dependent patients receiving methadone, we evaluated whether caller behavior differed for patients who reported continued drug use.
Methods: The Recovery Line (RL) is comprised of educational modules that present the basic principles of cognitive behavioral therapy. Each RL section includes learning and activity sections to directly implement skill based learning. Patients were asked to call daily, and had unlimited access to the system for 4 weeks with free choice of system navigation. The RL assesses three domains at the beginning of each call ("How are you doing today?" "Have you taken your methadone in the past 24 hours?" and "Have you used since your last call?"). Analyses used descriptive statistics and mixed-method ANOVA with autoregressive covariance matrix to evaluate call behavior outcomes based on reported drug use controlling for caller.
Results: Patients (n = 18) made a mean (SD) of 11.4 (8.7) calls with a mean call length of 10.6 min (4.2). 83% (15) reported drug use on one or more calls, and 50% (9) reported use on 4 or more calls. Drug use was reported for 32% of calls (74 of 224). Compared to calls in which patients denied drug use, those in which patients reported use were longer (p=.05; 10.8 vs. 8.8 min), and more likely to occur during hours their methadone clinic was closed (p=.001), but did not differ on the time since the patient last called the RL (p=.13). On calls that reported drug use, callers were more likely to access modules related to understanding drug use patterns and dealing with withdrawal and cravings (p's<.001).
Conclusions: Findings indicated that patients commonly reported drug use when using the RL, and suggest that automated treatment systems can successfully engage such patients in relevant treatment interventions. Additional evaluation of within patient changes in system and drug use behavior isneeded.
Financial Support: NIDA R01034678

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SOCIAL WORK STUDENTS' ATTITUDES TOWARDS APPROACHES TO ALCOHOL OR OTHER DRUG TREATMENT.

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Aims: Given the increasing numbers of people in need of treatment for AOD misuse/abuse and the concomitant likelihood that social worker caseloads currently reflect this increase, an analysis of social work student attitudes towards approaches to AOD treatment is warranted. The aim of this study is to explore attitudes towards abstinence-oriented and harm reduction approaches.
Methods: A convenience sample of fifteen, MSW-level social work students who completed an Internet-delivered Consequence Analysis (CA) intervention designed to shift attitudes towards a greater openness to harm reduction approaches to practice, participated in hour-long follow-up interviews. Of those assigned to the CA phase of the larger, mixed method study, four whose post-intervention ratings changed most from abstinence to harm reduction, three whose changed most from harm reduction to abstinence, four whose changed least from abstinence to harm reduction, and four who changed least from harm reduction to abstinence were interviewed. The transcripts were analyzed by taking grounded theory approach to the texts, facilitated by ATLAS.ti computer software.
Results: The central category emerging from the data was perspective-taking, or reference to how an approach would affect the client, clinician, or both. Perspective-taking was related to how a participant perceived his or her knowledge base. Those firmly abstinence-oriented perceived their knowledge bases as unreliable and were clinician-centered in their evaluations of treatment approaches. Those who shifted towards abstinence or harm reduction perceived their knowledge bases as unreliable, but were largely client-focused in responding. Finally, those firmly harm reduction-oriented perceived their knowledge bases as reliable and were client-focused.
Conclusions: The conditional relationships between perspective and perceived substance use treatment knowledge bases highlight the importance of strengthening social work education to prepare students to adopt a client-centered approach to practice with people with AOD problems, such that a respect for the value of a harm reduction approach is inevitable.
Financial Support: NIDA (5T32 DA07233)

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RELATIONSHIP BETWEEN SLEEP PROBLEMS AND HEAVY/ PROBLEM SUBSTANCE USE IN PRIMARY CARE PATIENTS.

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Aims: Insomnia effects between 10-50% of patients attending primary care. Insomnia is associated with psychiatric disorders (i.e. anxiety, depression), decreased quality of life, and impairments in work functioning (Roth, 2007). The present study examines the relationship between heavy problem substance use (HPS) and sleep problems in a primary care setting.
Methods: Patients receiving outpatient care at a large urban hospital completed a 15-minute computer-directed survey (HealthCheq) about demographics, recent substance use and other health behaviors, including sleep. The CAGE and T-ACE for alcohol and drugs, as well as quantity/frequency items, were used to categorize participants as positive (N=953; 29.18%) or negative (N=2313; 70.82%) for HPS. Sleep items focused on such things as trouble staying asleep, difficulty falling asleep, and taking something to help them sleep.
Results: The sample (N= 3266) was primarily African-American (71.6%) female (72.8%) with a mean age of 46.5 years old (SD=12.27). Over one-third (37.3%) of males and 18.6% of females screened positive for HPS use. HPS users were more likely than non-users to report trouble falling asleep (67.1% vs. 56.1%; $X2 = 33.35$, $p < .001$), trouble staying asleep (69.6% vs. 58.8%; $X2 = 32.96$, $p < .001$), and taking something to help them sleep (41.8 % vs.31.4%; $X2 = 36.64$, $p < .001$).
Conclusions: Findings support a link between heavy/problem substance use and sleep problems in primary care patients, though further research is needed to clarify the direction of causality. Careful screening of patients with sleep problems for alcohol/drug use is warranted as well as education about the role substance use may play as a potential contributing factor in sleep disturbance.
Financial Support: RO1 DA026091

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CRAVING FOR METHAMPHETAMINE IS NEGATIVELY ASSOCIATED WITH GRAY-MATTER VOLUME.

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Aims: Prospective studies show that craving for methamphetamine (MA) persists even after protracted abstinence from chronic use [1], and that craving levels predict subsequent drug use [2]. These studies suggest that the neurobiological mechanisms that promote drug craving are long-lasting and clinically relevant. Drug cues illicit brain activation in a neural network, that includes the orbitofrontal cortex, insula and anterior cingulate. As MA-dependent individuals have lower gray-volume than healthy control participants in brain regions implicated in craving [3], we hypothesized that greater craving for MA would be associated with lower gray-matter volume in components of fronto-limbic circuitry.
Methods: We measured gray-matter volume using voxel-based morphometry in 58 MA-dependent individuals who underwent high-resolution structural imaging during the first 4-7 days of abstinence from MA. Craving was measured during 1 of the first 5 days of abstinence using a self-report scale. Subjects were instructed to select, on a 10-point scale of 0 ("not at all") to 100 ("strongest ever"), the number that corresponded with their craving for "the past 24 hours."
Results: Whole-brain voxelwise analysis showed that individuals reporting stronger craving for MA had lower gray-matter volume in insula, orbitofrontal cortex, amygdala, occipital cortex, temporal cortex, and cerebellum (controlling for age, sex, frequency of MA use, and time since last MA use; $p < 0.05$ corrected).
Conclusions: The results suggest that individual variability in gray-matter integrity may be an important predictor of drug craving; however, more work is needed to determine whether variation in gray-matter integrity precedes or is induced by MA abuse.
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A NOVEL 5HT2C-SPECIFIC AGONIST/5HT2A-2B ANTAGONIST ATTENUATES PSYCHOMOTOR BEHAVIORS INDUCED BY METHAMPHETAMINE, OXYCODONE, AND THEIR COMBINATION.

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Aims: Serotonin 5HT2A and 5HT2C receptors are expressed and have relevant function in established drug reward circuitry. Opioids and stimulants are often abused concurrently. Although there are no approved medicines to treat psychosimulant abuse, a novel 5HT2C-specific agonist with 5HT2A-2B antagonist activity, (-)-trans-4-phenyl-2-dimethylaminotetralin (PAT), demonstrates preclinical efficacy to attenuate the hyperactivity effect of the stimulant amphetamine. It was hypothesized that (-)-trans-PAT would attenuate the effects elicited by an opioid, as well as, a combination of an opioid and a stimulant.
Methods: Experimentally naïve male, adult C57Bl/6J mice (n=138) were tested in a locomotor chamber under a camera connected to a tracking software package. Saline or (-)-trans-PAT were administered 10 minutes before treatment with methamphetamine and/or oxycodone, and mice were immediately placed in the activity field for a 60-min session.
Results: Methamphetamine and oxycodone produced dose-dependent increases in activity with highest and equivalent levels obtained at 3.0 mg/kg methamphetamine and 5.6 mg/kg oxycodone (~30,000 cm travelled versus ~8,000 cm following saline administration). Pretreatment with methamphetamine, resulted in a dose-dependent leftward and upward shift in the oxycodone dose-effect curve. High levels of activity (~30,000 cm) were obtained following administration of 1.7 mg/kg methamphetamine and 1.0 mg/kg oxycodone in combination. Administration of 10 mg/kg (-)-trans-PAT as a pretreatment attenuated hyperactivity in all groups.
Conclusions: Using a single molecule ([-]-trans-PAT) that possesses 5HT2C agonist activity together with 5HT2A-2B antagonism attenuated hyperactivity induced by oxycodone or methamphetamine, as well as, a combination of the two drugs, suggesting a novel pharmacotherapeutic approach for stimulant, opioid, and poly-drug abuse.
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SUPPORT, TRAUMATIZATION, AND EMPLOYMENT DIFFERENCES IN DRUG COURT OUTCOMES.

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Aims: Adult drug treatment court (ADTC) outcomes in relation to social support, trauma, and employment are poorly understood. We examined these outcomes and related factors.
Methods: Bivariate analysis using chi square and t-test assessed the following outcomes: substance abuse, arrests, health problems, emotional problems, social risk problems, and recovery environment risk using Global Appraisal of Individual Need data collected as part of a multi-site study examining drug use, recidivism, service utilization and treatment. ADTC clients from twelve sites were included (N=666 male, 915 female). Independent variables included: gender, race, age, years of education, income, partner status, employment, social support, traumatization, and traumagenic factors.
Results: Social support was associated with a decreased likelihood of arrest ($p<.033$), substance abuse ($p<.001$), recovery environment risk ($p<.001$) and social risk index ($p<.001$). Victimization within the past year was associated with increased substance use ($p<.001$), social risk problems ($p<.008$), and recovery environment risk ($p<.001$). Employment within the past year was associated with decreased recovery environmental risk ($p< .024$) and substance use ($p<.001$). Female gender was associated with an increased likelihood of reduction in substance abuse ($p<.038$).
Conclusions: Desireable ADTC outcomes derive from: Social support related to 4 of 6 outcomes. Victimization history related to 3 of 6 outcomes. Employment related to 2 of 4 outcomes. Client victimization related to ADTC outcomes. Addressing victimization and employment appear important to improve outcomes, as supported by these findings.. Future analyses will examine whether these findings are robust in a multivariate analysis, controlling for trauma-informed treatment as well as a rasch based outcome model to determine factors that affect multiple outcomes.
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EFFECT OF METHYLPHENIDATE PREEXPOSURE ON METHYLPHENIDATE-INDUCED CONDITIONED TASTE AVOIDANCE.

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Aims: Abuse liability is impacted by the rewarding and aversive properties of the drug, such that the former increases intake while the latter limits it. These two constructs vary independently, and their balance is altered by many factors, including drug history. Exposure to abusable compounds tends to weaken their aversive properties which in turn increases the likelihood of abuse. Although such attenuation has been reported for many psychostimulants, it is unknown whether such effects occur with methylphenidate (MPH, widely prescribed for treatment of ADHD) following chronic clinical use. To address this issue, we assessed the effect of preexposure to MPH on MPH conditioned taste avoidance (CTA; an index of the aversive effects of drugs) in adults. It was predicted that animals preexposed to MPH would exhibit attenuated MPH CTA.
Methods: Adult (PND 75-115, n = 68) male Sprague Dawley rats were preexposed to 0 or 18 mg/kg MPH, IP, every 4th day for five injections. During CTA conditioning, subjects received 20-min access to saccharin followed by injection of MPH (0, 10, 18 or 32 mg/kg; IP) every 4th day for four conditioning trials and then a final two-bottle avoidance test. Consumption data were analyzed with repeated-measures and one-way ANOVAs, followed by tests of simple effects as needed.
Results: In support of our hypothesis, subjects preexposed to MPH exhibited attenuated CTA compared to controls. Specifically, MPH-preexposed subjects drank significantly more saccharin than vehicle-preexposed subjects on Trials 2 – 4. Further, in the two- bottle test, MPH preexposed groups receiving 10 or 18 mg/kg during conditioning drank a higher percentage of saccharin than vehicle-preexposed controls.
Conclusions: As with many drugs of abuse, preexposure to MPH attenuated its aversive effects. Results suggest attenuation of MPH's aversive effects following chronic use may increase its abuse potential given the shift in the balance of reward/aversion.
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EXAMINING THE RISK FOR DEVELOPING ALCOHOL-RELATED PROBLEMS AMONG ADULT CHILDREN OF ALCOHOLICS.

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Aims: Research shows that alcohol use (quantity and frequency) is a prevalent problem on college campuses resulting in a number of alcohol-related problems (e.g., Mares, et al., 2011); however some young adults are more prone to problems than others (e.g., Borden et al., 2011). The goal of this study is to examine the risk factors that predict alcohol-related problems. One such risk factor is having an alcoholic parent, termed Adult Children of Alcoholics (ACOA). Another risk factor of interest is affect lability, described by an inability to regulate mood. Both ACOA (e.g., Kelley et al., 2010) and affect lability (e.g., Simons, Carey, & Gaher, 2004) have been linked individually to increased alcohol use and problems, but no study to date has looked at how these variables interact to explain problems.
Methods: Participants were (N = 206) undergraduate students, mostly female (55.8%) and Caucasian (58.3%) with a mean age of 22.81 years. Participants completed a survey of questionnaires assessing the quantity and frequency of their alcohol consumption, alcohol-related problems, affect lability, and the Children of Alcoholics Screening Test. Participants retrospectively responded to questions regarding their parent's alcohol use and (n = 44) were classified as an ACOA.
Results: Bivariate correlations revealed significant relationships between use, frequency, ACOA status, and affect lability with alcohol-related problems, ps < .05. Controlling for use, frequency, and gender, a multiple regression analysis revealed that ACOA status significantly predicted alcohol-related problems ($p < .01$, $R2 = .425$). Further, ACOA status moderated the effect between affect lability and problems, $\beta = 626$, $p < .01$.
Conclusions: Higher affect lability predicted more alcohol-related problems and this effect was strengthened for those classified as an ACOA, making them more vulnerable to alcohol-related problems. These results have practical implications on the prevention of risky alcohol use among young adults. Further research is needed to determine the causal mechanisms involved.
Financial Support: This work was supported by a fellowship from the Society of Public Health Education.

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PROGNOSTIC RELEVANCE OF DOPAMINE BETA-HYDROXYLASE LEVELS ON DISULFIRAM TREATMENT AT HIGHER DOSES OF COCAINE DEPENDENCE IN METHADONE-STABILIZED PATIENTS: A SECONDARY ANALYSIS.

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Aims: Disulfiram (DSF), an inhibitor of dopamine (DA) beta-hydroxylase (DBH), which converts DA to norepinephrine, has shown some efficacy in treating cocaine (COC) dependence. Studies have indicated that treatment response among individuals may be influenced by DBH-associated differences. This study reports on secondary analyses examining the prognostic relevance of DBH levels in a clinical trial of disulfiram at higher doses for treating cocaine dependence in methadone-stabilized participants.
Methods: Data were obtained from 43 cocaine- and opioid-dependent volunteers participating in a 14-week, double blind, randomized, placebo-controlled clinical trial. Methadone-stabilized (weeks 1-2) participants were randomized to receive disulfiram at 0, 250, 375 or 500 mg/day (weeks 3-14) and underwent weekly cognitive behavioral therapy. Thrice-weekly urine samples were obtained. Blood samples drawn prior to disulfiram treatment were assayed for DBH enzyme levels.
Results: No significant baseline differences in demographics or DBH levels occurred across medication groups. At baseline, no differences in cocaine use occurred by medication group in those with either low or high DBH levels ($p>0.05$). In those with low DBH levels, there was no difference over time in cocaine positive urines in any disulfiram group relative to placebo ($p>0.05$). In those with high DBH levels, however, a trend toward a greater decrease in cocaine use in the 500 mg group relative to placebo was noted (OR= 0.96, $p=0.1025$).
Conclusions: In our study DBH level did not differentially impact treatment response to DSF higher doses in cocaine-dependent, methadone-stabilized participants.
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CHEMICAL MODIFICATIONS TO ALTER MONOAMINE RELEASING ACTIVITY OF PHENMETRAZINE ANALOGS AS POTENTIAL TREATMENTS OF STIMULANT ADDICTION.

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Aims: According to the dual deficit model of stimulant addiction, dopamine (DA) and serotonin (5-HT) deficits contribute to withdrawal, drug craving, and relapse. Dual DA/5-HT releasers would provide the necessary stimulant-like properties via DA release, and its ability to release 5-HT would reduce its abuse liability. Previous data with universal releaser PAL287 suggest that 5-HT elevations counteract DA's reinforcing effects. Similarly (+)-phenmetrazine, a potent DA releaser with weak 5-HT releasing activity, selectively suppresses cocaine vs food maintained responding. Hence the aim was to synthesize and evaluate analogs of phenmetrazine to understand the structural requirements for DA and 5-HT releasing activity and to afford a superior dual DA/5-HT releasing agent for treatment of stimulant addiction.
Methods: Electron-withdrawing, donating and bulkier substituents on the phenyl ring of phenmetrazine were incorporated as racemic as well as enantiopure forms. Positional isomers of the alkyl substituent on the morpholine ring were also synthesized. These ligands were evaluated for DA/5-HT release ability. Standard transporter uptake inhibition and superfusion release assays using synaptosomes prepared from rat brain were used.
Results: In this study 3'-substituted compounds were DA releasers while some 4'-substituted compounds were DA reuptake inhibitors. Importantly 3'-chloro analog (PAL594) of (+)-phenmetrazine afforded DA as well as 5-HT releasing activity at EC50 values of 27nM and 301nM, respectively. Two compounds, PAL730 and PAL738, are more potent DA/5-HT releasers than phenmetrazine, with PAL738 exhibiting DA and 5-HT releasing activity at EC50 values of 58nM and 23nM, respectively.
Conclusions: Results contribute to the evidence supporting the potential utility of monoamine releasers as candidate treatments for stimulant addictions.
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SELF-ADMINISTRATION OF OXYCODONE ALONE OR AS A MIXTURE WITH THE KAPPA AGONIST, SALVINORIN A, BY MONKEYS UNDER A PROGRESSIVE RATIO SCHEDULE OF REINFORCEMENT.

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Aims: The incidence of prescription opioid abuse has increased in recent years. We have recently determined that the kappa opioid agonist, salvinorin A (SVA), can punish self-administration of the mu agonist, remifentanil. To extend these findings to a prescription opioid of demonstrated abuse potential, the current study was designed to determine if SVA, when contingently administered with the mu agonist, oxycodone, could reduce the reinforcing effectiveness of oxycodone.
Methods: Male rhesus monkeys (n=3) were trained to self-administer cocaine (0.1 or 0.2 mg/kg/inj) under a progressive-ratio (PR) schedule of reinforcement with alternating saline sessions. Once self-administration was stable, tests were inserted into the sequence. Test conditions consisted of a range of doses of oxycodone alone (0.006-0.1 mg/kg/inj) or oxycodone mixed with a dose of SVA (0.003 mg/kg/inj).
Results: Oxycodone self-administration resulted in biphasic dose response functions, with the highest breakpoint occurring at the 0.05 mg/kg dose in all three monkeys. Combining SVA with oxycodone resulted in rightward and downward shifts in the dose-response functions for oxycodone, indicating a decrease in both the potency and effectiveness of oxycodone as a reinforcer.
Conclusions: Our findings demonstrate that SVA, when contingently administered with oxycodone, decreases the reinforcing effectiveness of oxycodone under the current PR schedule conditions. Adding kappa agonists to prescription opioids may be a viable abuse-deterrent formulation strategy.
Financial Support: This research was supported by grants R01-DA-027666 to KBF and R01-DA-018151 to TEP from the National Institute on Drug Abuse.

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PROGRESSIVE RATIO RESPONDING FOR MORPHINE IS DIFFERENTIALLY ALTERED IN THE PRESENCE OF CHRONIC PERIPHERAL NEUROPATHY IN MALE VS. FEMALE C57BL/6 MICE.

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Aims: Clinical management of chronic pain with prescription opioids remains a challenge due to concerns about opioid-induced dependence and addiction. Sex-differences in pain sensitivity, opioid analgesia, and reinforcing effects of opioids are observed in rodents. The purpose of our study is to test the hypothesis that the presence of paclitaxel-induced chronic peripheral neuropathy will differentially alter the sensitivities of male and female mice to morphine-induced reinforcing effects.
Methods: Male and female C57Bl/6 mice were implanted with indwelling catheters and trained to self-administer morphine under a progressive ratio (PR) schedule of reinforcement. Following stable responding, mice were treated with saline or paclitaxel (PAC) and tested for morphine (0.01-0.1 mg/kg/inf) responding under PR.
Results: PAC treatment produced higher breakpoints for morphine that increased progressively with the development of allodynia in male but not in female mice. A significant upward shift in the dose-effect curve for morphine was observed in the PAC-treated male mice. While only the PAC-treated male mice demonstrated an increase in motivation to respond for morphine, increases in the PR responding for morphine were observed in both in the saline- and PAC-treated female groups. The cumulative records from the self-administration sessions displayed marked differences in the pattern of drug-taking behavior in the PAC versus control male mice. Further, PAC-treated male mice displayed increased intake of the prescription opioid morphine in the state of chronic pain compared to their saline-treated counterparts.
Conclusions: The reinforcing effects and the motivational salience of morphine are altered by the presence of paclitaxel-induced peripheral neuropathy with male mice displaying greater sensitivity to these effects compared to female mice. Overall, these results may have implications for the understanding of potential sex differences in the clinical management of pain and the gender-dependent abuse liability of prescription opioids in humans.
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PATTERNS OF CRACK USE AMONG DRUG-USING FEMALES IN MEXICO CITY.

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Aims: Mexico has seen a rise in crack use yet there remains a gap in the knowledge base regarding the practice of smoking crack. This is compelling as crack use is a significant public health concern due to associated HIV risk. Even less is known regarding patterns of initiation and escalation of crack use among Mexican women. This presentation utilizes gender role theory to examine women's distinct pathway to crack use initiation.
Methods: In-depth semi-structured ethnographic interviews and observations were conducted with 150 male and female adult current crack users from neighborhoods (colonias) in three delegaciónes (boroughs) in México DF : Iztapalapa, Coyoacán and Cuauhtémoc. For the purpose of this study, only the data on female crack users was analyzed (n=42).
Results: Findings indicate that crack use among women was often initiated in the presence of romantic partners who through the process of observation learned how to prepare, smoke and use specific paraphernalia. Female participants' access as well as consumption of crack was largely facilitated by their male partners who would often decide how much crack they were willing to share or buy for the women. Many participants reported experiences of past trauma or depression that led to the escalation of their drug use. For those that were daily users, exchanging sex was described as a viable way to have access to crack but also placed them at high risk for violence and STDs.
Conclusions: With the diffusion of crack use in Mexico, studies are needed to understand the distinct patterns of initiation and use to develop culturally responsive interventions. Specifically, our findings regarding crack using women in Mexico City have implications for the development of gender based interventions and community approaches that take women's unique drug use trajectories into account.
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ALTERATION OF CIRCULATORY CYTOKINE LEVELS IN ALCOHOL-USE DISORDER PATIENTS WITH OR WITHOUT COMORBID MAJOR DEPRESSION.

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Aims: Evidence suggests that major depression (MD) is accompanied by increased production of pro-inflammatory cytokines, including interleukin (IL)-6, tumor necrosis factor (TNF)-α and interferon (IFN)-γ, and a dysregulated immune system. This is, however, less studied among alcohol-use disorder (AUD) patients. We aimed to assess the circulatory cytokine levels in AUD patients with or without MD and to assess the influence of AUD on cytokine levels in MD.
Methods: A consecutive sample of AUD inpatients (N=176) at eight alcohol treatment centres in Kathmandu, Nepal was administered structured questionnaires to assess socio-demographic and alcohol-use characters and to establish DSM-IV diagnoses of AUD and MD. Using Bio-Plex Pro Human Cytokine 27-plex kit, we assayed 27 cytokines. Six pro-and-anti-inflammatory cytokines shown to be relevant in depression disorders are presented.
Results: AUD patients with MD co-morbidity compared to those with only AUD had higher serum levels of IL-6 ($p = 0.02$), TNF-α ($p = 0.02$), IFN-γ ($p < 0.01$) and RANTES ($p = 0.01$), but the anti-inflammatory cytokines (IL-1Ra and IL-10) were unaltered. Smoking and drug abuse were associated with low IL-10 levels and high IL-6 levels. For TNF- α, there was a significant interaction between MD and using alcohol as eye opener (Beta= 0.5; $P<0.001$); for RANTES significant interaction was observed between MD and average units of ethanol consumed daily (Beta= 0.3; $P<0.01$).
Conclusions: The altered functioning of the immune system in AUD patients with MD seems to resemble that seen in depressed patients without an AUD. MD as a comorbidity,as well as AUD severity influence the cytokine levels and significant interaction effects between them indicate a possible link between AUD and MD.
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NON-MEDICAL USE OF PRESCRIPTION DRUGS AMONG HIV-POSITIVE INDIVIDUALS TAKING ANTIRETROVIRAL THERAPY.

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Aims: The non-medical use (NMU) of prescription drugs is increasing dramatically. The HIV-positive are at high risk due to co-occurring pain, mental health, and substance use issues. An increased understanding of the factors associated with prescription drug misuse in HIV may help clinicians balance patients' access and legitimate use of such drugs and reduce the risks for abuse and addiction.
Methods: We assessed 294 HIV-clinic patients who were prescribed antiretroviral therapy in San Francisco. We compared participants who reported NMU of prescription drugs (past month use of methadone, other opiates/analgesics, barbiturates, and/or sedatives/hypnotics/tranquilizers without a prescription) to those who did not on demographics, other drug use, psychiatric/medical conditions, antiretroviral adherence, and quality of life in bivariate analyses, and then put all significant variables into a logistic regression.
Results: 32 (11%) reported past month NMU of prescription drugs. Alcohol use severity ($Z=-3.45$, $p=0.001$), use of heroin ($X^2=20.58$, $p<0.001$), cocaine ($X^2=12.06$, $p<0.001$), amphetamines ($X^2=5.02$, $p=0.025$), and cannabis ($X^2=4.69$, $p=0.03$), general health perceptions ($t=2.90$, $p=0.004$), cognitive functioning ($t=3.15$, $p=0.002$), health distress ($t=2.29$, $p=0.023$), depression ($Z=-2.63$, $p=0.009$), and medication side effect severity ($Z=-2.90$, $p=0.004$) were associated with NMU in bivariate analyses. Medication side effects ($\beta=1.08$, 95%CI: 1.02-1.14, $p=0.007$) and cognitive functioning ($\beta=0.96$, 95% CI: 0.93-0.99, $p=0.025$) remained significant in regression analysis.
Conclusions: This analysis provides important information about NMU of prescription drugs among HIV-positive individuals. NMU of prescription drugs may serve to aid coping with medication side effects and decreases in cognitive functioning. Results support that both substance use programs and behavioral self-management skills are important components of future interventions. Promising intervention models will be those that integrate prevention, mental health, and substance use services.
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COCAINE-CONDITIONED LOCOMOTOR RESPONSE: MODULATING ROLES OF ENVIRONMENTAL CONTEXT AND NEURAL PLASTICITY.

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Aims: Compounds known to modulate neural plasticity-associated signaling cascades were evaluated for their ability to affect the acquisition and expression of cocaine-conditioned locomotor response.
Methods: Cocaine (40 mg/kg) was administered to different groups of Swiss-Webster mice via intraperitoneal injection (i.p.), in either a locomotor activity testing apparatus or the home cage, 2 hours following an activity test under saline. Mice placed in the testing chambers were given 30 minutes to explore freely and locomotion was monitored using a Digiscan photocell apparatus. A conditioned effect of cocaine was inferred by an increase in horizontal activity counts relative to home cage cocaine controls during a test in the same apparatus on the following day. For testing of effects on expression of the conditioned cocaine effect, mice were administered haloperidol (0.05-1 mg/kg), dizocilpine (0.01-0.25 mg/kg), nifedipine (0.1-10 mg/kg), cyclohexamide (2.5-10 mg/kg), or vehicle, prior to placement into the activity chambers on the test day. The same compounds were administered prior to the acquisition day in a separate set of studies.
Results: Haloperidol (0.25-1 mg/kg) inhibited expression of the cocaine-conditioned locomotion, though failed to alter acquisition of the behavioral response. Dizocilpine (.05-0.25 mg/kg) attenuated acquisition and exacerbated expression. Nifedipine had no effect on the conditioned locomotor response. Cyclohexamide (2.5-10 mg/kg) attenuated acquisition of the conditioned response.
Conclusions: The ability of these compounds to inhibit or exacerbate the conditioned behavior suggests that plasticity-dependent signaling pathways mediate associations of context following acute cocaine exposure and are necessary for the acquisition and expression of the cocaine-conditioned locomotor response.
Financial Support: n/a

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PRECLINICAL EVALUATION OF JPC-141 AS A NOVEL TREATMENT FOR METHAMPHETAMINE ABUSE.

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Aims: Methamphetamine (METH) abuse continues to present a formidable challenge to health care in the United States. Lobeline, an alkaloidal constituent of *Lobelia inflata*, has efficacy in preclinical studies, attenuating the reinforcing properties of METH via interaction with the vesicular monoamine transporter-2 (VMAT2). Chemical defunctionalization of lobeline afforded lobelane, which exhibited greater selectivity for VMAT2. Tolerance developed to the effect of lobelane to inhibit the behavioral effects of METH. Substitution of the piperidine ring of lobelane with a piperazine ring and translocation of the 2,6-diphenethyl side chain to the 1,4 position afforded a novel analog series with enhanced water-solubility.
Methods: An analog in this series, JPC-141, was assessed for its ability to inhibit [^{3}H]dihydrotetrabenazine (DTBZ) binding to and [^{3}H]dopamine (DA) uptake at VMAT2. Affinity for the human ether-a-go-go (hERG) channel was also determined, as was efficacy of JPC-141 in reducing METH-induced locomotor sensitization.
Results: JPC-141 retained the affinity of lobelane for both the [^{3}H]DTBZ binding site (Ki=1.07±0.25 μM) and [^{3}H]DA uptake site (37±0.5 nM) on VMAT2. JPC-141 displayed 350-fold greater affinity for VMAT2 than the plasmalemma dopamine transporter (Ki=12.8±4.46 μM), suggesting low abuse liability. JPC-141 also exhibited greater than 30-fold selectivity for VMAT2 versus the hERG channel (IC50=3.19±0.327 μM), suggesting low potential for cardiotoxicity. When administered at a dose of 30 mg/kg (s.c.), JPC-141 markedly attenuated (61%) METH-induced locomotor sensitization, while having no effect in controls receiving repeated saline.
Conclusions: These early preclinical data indicate that structural modification of lobelane affords novel compounds which retain the desired pharmacological properties and provides greater druglikeness. Thus, JPC-141 represents a promising preclinical lead in the development of a pharmacotherapeutic for METH abuse.
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THE INVOLVEMENT OF THE CNR1 GENE IN IMPULSIVITY AND STRESS RESPONSE IN ALCOHOL-RELATED BEHAVIORS.

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Aims: Research showed a SNP (rs2023239) of the CNR1 gene resulted in different levels of CB1 receptor binding, differential alcohol cue-elicited brain activation in brain regions related to reward and dependence, and greater reward following alcohol consumption. However, the rates of alcoholism are similar between the genotypes. Most likely this variation is related to a specific subtype of alcoholism. In this study, our aim was to determine if this CNR1 SNP is related to increased reward from the thrill of novelty seeking or the abatement of the stress response.
Methods: To test our hypothesis, impulsivity was measured using self-report and a Go/No Go paradigm. After inducing social stress (TSST), we measured physiological and subjective stress responses. Finally, we assessed alcohol craving.
Results: There was a trend that those with the risk allele scored higher in harm avoidance (M = 52.17, SD = 18.33) than those without (M = 44.25, SD = 20.60), $t(45.50) = -1.69$, $p = .098$. Harm avoidance can be related to anxiety sensitivity (measured by the BAI and Trait Anxiety in the STAI), which was determined using regression analysis to predict stress response throughout the paradigm as measured physiologically (skin temperature and conductance) and subjectively (State Anxiety, SRS, and VAAS). Further, stress response (skin temperature) significantly predicted participants' scores on drinking behaviors, measured by the Temptation and Restraint Inventory, which, in turn, predicted the severity of alcohol dependent behaviors (ADS). Conversely, those that scored higher in novelty seeking had higher skin temperatures throughout the experiment than those that scored lower, indicating that novelty seekers experienced less anxiety ($F(1,69) = 10.17$, $p = .0020$).
Conclusions: In conclusion, these data indicate that the increased reward felt by those with the risk allele may be a result of reduced anxiety, while other genetic influences may explain alcoholism subtypes related to novelty seeking.
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PHARMACOGENETICS OF BUPRENORPHINE THERAPY OF COCAINE ADDICTION.

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Aims: To identify genetic markers of the opioidergic system that modulate therapeutic response to buprenorphine treatment of cocaine addiction.
Methods: Cocaine-dependent subjects (N=302) with past-year opioid dependence/abuse, or past-year opioid use and a history of lifetime opioid dependence were randomly assigned to one of three medication conditions provided on a platform of naltrexone: daily 4 mg buprenorphine, 16 mg buprenorphine, or placebo, for 8 weeks and had once-weekly cognitive behavioral therapy in the CTN-0048 Cocaine Use Reduction with Buprenorphine clinical trial. DNA (N=234) was genotyped for 13 variants in six genes. Treatment efficacy was evaluated by the percent cocaine positive urines per two week period.
Results: Similar but modest reductions in percent positive urines were observed in the 4mg and 16mg buprenorphine groups. Therefore, the 4mg and 16mg groups were combined and contrasted with the placebo group using repeated measures ANOVA. Experiment-wise significant interactions of variant x treatment were found for two variants of the proopiomelanocortin (POMC) gene (both p=0.003). In the POMC rs1009388 C allele-carrier group, placebo increased positive urines from 57% to 60%, while the buprenorphine decreased positive urines from 43% to 39%, with no difference between placebo and buprenorphine for the GG group.
Conclusions: These data implicate POMC peptides and the pathways in which they participate as targets for future studies on cocaine addiction therapy.
Financial Support: NIH/NIDA P50 DA018197 (TK, DN), NIH/NIDA U10DA020024 (RW), for DN through MD Anderson's Cancer Center Support Grant NIH/NIDA DA026120, and the Toomim Family Fund. This material is the result of work supported with resources and the use of facilities at the Michael E. DeBakey VA Medical Center, Houston, TX.

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BENZODIAZEPINE USE AMONG A SAMPLE OF CHRONIC PAIN PATIENTS PRESCRIBED OPIOIDS.

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Aims: Previous research documents harms from long-term benzodiazepine (BZD) use, and there is little evidence to support the use of BZD in the treatment of chronic non-cancer pain. The aim of this study was examine BZD use in people prescribed opioids for chronic pain.
Methods: Data were collected from baseline telephone surveys (n = 1107) as part a prospective cohort study of people prescribed opioids for chronic non-cancer pain. Those reporting no BZD use in the past month were compared with less than daily, and daily BZD users. General demographics, mental and physical health co-morbidity, pain severity, interference and coping, and health service utilisation were examined.
Results: Sixty-two percept of the sample report lifetime BZD use; 33% (n = 362) reported past month use. Of those using BZDs in the past month, 168 (46%) reported less than daily use, and 194 (54%) reporting daily use. Univariate analysis found benzodiazepine use was associated with longer durations of opioid prescribing, greater pain interference and reduced pain coping. BZD use was associated with greater utilisation of ambulance and hospital emergency services. Those reporting past month BZD use were more likely to report a history of overdose, and also more likely to meet criteria for moderate to severe depression and anxiety. After controlling for age, gender, anxiety, depression, number of chronic conditions and length of opioid prescribing, BZD use was associated with more ambulance and emergency presentations in the past month ($p < .05$).
Conclusions: Past month BZD use appears to be associated with more severe physical and mental health disability, and higher utilisation of health services. A high prevalence of BZD use was observed. It will be important to examine long-term outcomes to explore the contribution of BZD use to harms.
Financial Support: NHMRC Project grant 1022522; SN, BL and LD are supported by NHMRC Fellowships.

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EXPOSURE TO FLUOXETINE DURING ADOLESCENCE INCREASES SENSITIVITY TO THE REWARDING EFFECTS OF COCAINE IN ADULTHOOD.

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Aims: Pediatric depression was not well recognized until relatively recently. Now we know that major depressive disorder (MDD) exists in children and adolescents, that it is also a common condition, and that it can have negative consequences that often extend into adulthood. It is estimated that children and adolescents who suffer from MDD are likely to develop conduct and anxiety disorders, and that 20-25% eventually develop substance abuse disorder. Consequently, this has resulted in a disproportionate increase in the prevalence of antidepressants prescribed to populations below 20 years of age. Despite the heightened rates in antidepressant use, little is known about the long-term clinical and neurobiological adaptations resulting from antidepressant treatment during periods prior to adulthood.To address this issue at the preclinical level,we examined whether Fluoxetine (Prozac) exposure during adolescence results in long lasting changes in sensitivity to the rewarding effects of cocaine.
Methods: Male C57BL/6 mice were exposed to Prozac (20 mg/kg/day) during adolescence (postnatal days [PD] 35-49) and were later assessed in adulthood (PD 70+) on behavioral responsivity to cocaine (0, 2.5, 5, 10, or 20 mg/kg) place conditioning (CPP).
Results: Here we show that mice pre-treated with Fluoxetine (20 mg/kg/day) during adolescence (PD35-49), displayed enhanced preference for environments previously paired with moderately low doses of cocaine (5 or 10 mg/kg), when compared to saline pre-treated controls.
Conclusions: Together, our findings suggest that exposure to Fluoxetine during adolescence increases sensitivity to the rewarding properties of cocaine, as measured by CPP, later in life.
Financial Support: NIDA

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A NOVEL MEASURE OF ASSESSING THE FREQUENCY AND ROUTE OF ADMINISTRATION OF VARIOUS SUBSTANCES OF ABUSE.

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Aims: To develop an assessment tool that accounts for novel substances of abuse while ascertaining information regarding prevalence and administration method of various substances.
Recently, there has been a proliferation of "legal highs" available on the Internet. These legal synthetic substances, known as "research chemicals," mimic the effects of illicit drugs. Among these, "bath salts" and synthetic cannabis have led to an increase in calls to US poison control centers by the thousands. There is a need for a substance use measure that accounts for such dangerous chemicals of abuse. With this in mind, we created the Substance Use Frequency and Administration Method Scale (SUFAMS).
Methods: Undergraduate students (N = 494, M age = 18.79, SD age = 1.93, 81.4% Caucasian, 64% Female) at a large public university completed an online survey that included the Drug Use Disorders Identification Test and SUFAMS.
Results: We assessed the lifetime prevalence of the use of cannabis (38.3%), synthetic cannabis (e.g. "spice") (9.1%), synthetic cathinones ("bath salts") (1.4%), MDMA (6.7%), dissociatives (2.9%), psychedelics (5%), non-prescription stimulants (1%), cocaine (2.5%), and non-prescription opiates (1.9%). We also assessed the lifetime prevalence of the off label use of prescription stimulants (9.5%), prescription opiates (7.3%), and prescription sedatives (4%). The frequency questions of the SUFAMS indicated high construct validity with the DUDIT's questions regarding drug use frequency. The most common methods of administration were smoking (cannabis, synthetic cannabis), oral (synthetic cathinones, MDMA, dissociatives, psychedelics, prescription and non-prescription stimulants, prescription and non-prescription opiates, prescription sedatives), and intranasal (cocaine).
Conclusions: This study provides a novel measure for assessing substance use frequency and administration methods among well-known and novel substances of abuse. Public health implications will be discussed.
Financial Support: K24AA019707

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PARENT TOBACCO USE, MONITORING, AND IMPULSIVE DECISION MAKING: PREDICTORS OF POST TREATMENT YOUTH SUBSTANCE USE.

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Aims: While contingency management(CM) interventions are effective in decreasing youth substance use, this effect is short-term. Poor parent monitoring and tobacco use predict youth substance use but their role and the role of parent impulsive decision making in substance use relapse is unknown. This study examined the influence of parent impulsive decision making and tobacco use on parent monitoring and the treatment related changes in parent monitoring on post treatment youth substance use.
Methods: Participants included 230 youths aged 12–18years who abused either alcohol, marijuana or both, and their parent(s). Families participated in a 14-week randomized trial examining the efficacy of the addition of CM to MET/CBT intervention. Frequency of youth substance use was assessed using the Timeline Follow Back method. Parents self-reported their tobacco use and monitoring of youth behaviors. To measure impulsive decision making, parents completed a delay discounting task (degree of preference for smaller immediate over larger delayed rewards).
Results: A latent growth model for youth substance use frequency at discharge, 3, 6, and 9months was fit. Five predictors were then added: parent monitoring at intake/discharge, treatment condition, parent delay discounting, and parent tobacco smoking status(smoker/non-smoker). The final model fit well($X2(18, N=230)=17.55, p=.49$, RMSEA=.00). Poor parent monitoring at intake(B=.68) and higher parent delay discounting(B=.14) was associated with poor parent monitoring at discharge. Although treatment condition did not predict youth substance use post treatment, poor parent monitoring at discharge(B=.39) and parent tobacco use(B=.37) predicted the youth substance use intercept (more days of substance use during treatment) accounting for 31% of the variance. No variable predicted rate of change in substance use post treatment.
Conclusions: Addressing parent substance use and impulsive decision making and targeting parent monitoring may be beneficial in improving the maintenance of parent monitoring and reducing youth substance use long-term.
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THE CAUSAL EFFECT OF OPIOID SUBSTITUTION TREATMENT ON HIGHLY ACTIVE ANTIRETROVIRAL TREATMENT ADHERENCE.

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Aims: Opioid substitution treatment (OST) has been associated with enhanced uptake and adherence to highly active antiretroviral therapy (HAART), however previous HAART adherence is hypothesized to be a time-dependent confounder for the effect of OST on future HAART adherence. Our objective was to determine the impact causal effect of OST exposure on adherence to HAART among HIV-positive opioid dependent individuals.
Methods: Using a linked population-level database, we considered all HAART-eligible HIV-positive individuals ever accessing OST between January 1st, 1996 and March 31st 2010 in British Columbia, Canada. A marginal structural model was estimated using monthly-updated inverse probability of treatment weights (IPTW). We controlled for fixed and time-varying covariates, including age, gender, ethnicity, health authority of residence, calendar year, OST history at HAART eligibility, AIDS status, CD4 and prior HAART exposure in estimated IPTW.
Results: Among 12,349 HIV-positive individuals observed in BC between 1996 and 2010, 1,811(14.7%) accessed OST, and 1,337(10.8%) were eligible for our study. Subjects were 39% female, were of median age 35 (interquartile range:29-41) at HAART eligibility, and had a median of 6.8 years(2.9-11.1) of follow-up. During OST, individuals spent a median 55% (20%-84%) of the time on HAART, while out of OST individuals spent only 26%(7%-56%) of the time on HAART. The unadjusted odds of HAART adherence during OST exposure was 2.27(95% confidence interval:2.01-2.55), while the adjusted odds, estimated within the marginal structural model, was 1.95(1.71,2.23).
Conclusions: Our results demonstrate that access to OST doubles the odds of HAART adherence among opioid-dependent individuals with HIV. This study informs funding decisions for OST and strategies to increase HAART adherence.
Financial Support: NIH/NIDA grant no: R01-DA032551.

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THE MISUSE, ABUSE AND DIVERSION OF OPIOID REPLACEMENT THERAPIES AMONG STREET ABUSERS.

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Aims: Buprenorphine is a partial opiate agonist believed to offer significant treatment advantages over existing opioid replacement therapies (ORT), such as methadone. Community-based abuse liability studies are needed to complement clinical and laboratory data First, we estimate the overall prevalence of misuse (self-treatment) and abuse (euphoria), as well as diversion. We also examine the psychosocial characteristics and differences between methadone and buprenorphine.
Methods: Targeted sampling was used to recruit recent (n=706) persons who inject drugs (PWID), including those receiving some form of outpatient drug treatment (45%) in San Francisco, CA. Final sample matched previous studies in SF, including demographic (53% white, 79% male, 36% ages 30-44, 63% homeless) and behavioral (13% HIV+) characteristics.
Results: Approximately 75% were candidates for ORT, based on heroin and/or prescription opioid (540/706) use. Over 30% of opioid addicts reported nonmedical (either euphoria or self-treatment) use of methadone, compared to 9% for buprenorphine. The prevalence of abuse was higher for methadone (75%) than buprenorphine (10%). Conversely, the prevalence for misuse (1-% of abuse) was higher among buprenorphine (90%) than methadone (25%). More outpatient clients reported being treated with methadone (50%) than buprenorphine (10%). Among those receiving outpatient treatment and prescribed methadone, approximately 50% abused their own medication compared to virtually none (<1%) of those being treated with buprenorphine. The significant predictors of nonmedical use that differentiated between misuse versus abuse were being out-of-drug-treatment (AOR=2.6, 95% CI= 1.2-5.7), co-occurring depression (AOR=1.4, 95% CI= 1.2-2.5), PTSD (AOR=1.6, 95% CI= 1.1-2.1), and high withdrawal severity history (AOR=1.1, 95% CI=1.01-1.3). There were few differences in the risk factor profiles between buprenorphine and methadone.
Conclusions: There appears to be differences in abuse liability among street-level abusers, as well as a high rate of self-treatment using ORT.
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GENDER DIFFERENCES IN THE INFLUENCE OF CHILD SEXUAL ABUSE ON DRUG USE AND RELATED HEALTH RISKS DURING YOUNG ADULTHOOD: THE MODERATING EFFECTS OF DRD4.

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Aims: There is strong evidence for the association between child sexual abuse and drug use and related problems. The diathesis-stress model predicts that an individual's sensitivity to stressful life events depends on their genetic makeup. We test whether the DRD4 gene moderates the effect of child sexual abuse on health risks (drug use, violence, criminal behavior, depression) for white young adult women and men.
Methods: We use data from the National Longitudinal Study of Adolescent Health. Individuals with two long alleles are hypothesized to be more sensitive to their environment and therefore more likely to report risk outcomes if they experienced child sexual abuse. We also hypothesize that genetics will matter for men but not women.
Results: We find that child sexual abuse increases the odds of depression, criminal behavior, and drug use among white men but only for those with the risky gene variant. For women, sexual abuse increases odds of depression, criminal behavior, and drug use regardless of gene expression.
Conclusions: This study contributes to a more nuanced understanding of the gendered responses to child sexual abuse as well as the mechanisms that link child sexual abuse to health risks for young adult white men and women.
Financial Support: Support for this study was provided by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) funded University of Colorado Population Center (R24 HD066613). Additional support was provided to Kathryn M. Nowotny through the National Institute on Drug Abuse (NIDA) funded Interdisciplinary Research Training Institute at the University of Southern California (R25 DA026401). This research uses data from Add Health, a program project directed by Kathleen Mullan Harris and designed by J. Richard Udry, Peter S. Bearman, and Kathleen Mullan Harris at the University of North Carolina at Chapel Hill, and funded by the NICHD (P01 HD31921), with cooperative funding from 23 other federal agencies and foundations.

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REGION SPECIFIC SEXUALLY DIMORPHIC INTRACELLULAR RESPONSES AFTER COCAINE-INDUCED CONDITIONED PLACE PREFERENCE EXPRESSION.

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Aims: Sex differences in cocaine's behavioral effects and mechanisms of action have been widely reported. However, little is known about how sex influences intracellular signaling cascades that underlie the neuroplasticity involved with drug-environment associations. We investigated whether ERK/CREB/FosB intracellular responses in the mesocorticolimbic circuitry underlying cocaine environmental associations are sexually dimorphic.
Methods: Using a four day, unbiased and counterbalanced conditioned place preference (CPP) protocol, male and female Fischer rats were conditioned with 20mg/kg cocaine (i.p.). Rats were tested for a preference for the cocaine-paired environment in a drug-free state 24 hours after the last conditioning session. Locomotor responses were recorded during conditioning and CPP testing. After the CPP test, rats were sacrificed and brains were prepared for western blot analysis.
Results: CPP behavior was expressed in both males and females, but females were more active during the CPP test and after cocaine-treatment during conditioning. Males and females showed similar increases in phosphorylated extracellular regulated kinase (ERK) and ΔFosB protein levels in the Nucleus Accumbens, whereas sex differences were seen in the Caudate Putamen (CPu).
Conclusions: Our results suggest that similar to males, the ERK/CREB intracellular pathway in mesocorticolimbic regions regulates cocaine induced neuroplasticity in female rats. Additionally, cellular responses associated with the development of learned drug-environment associations may play an important role in sex differences in cocaine addiction and relapse.
Financial Support: This work was supported by DA12136, RR-024996, RR-03037 and PSC-CUNY.

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DEPOT NALTREXONE AS RELAPSE PREVENTION FOR OPIOID-DEPENDENT PAROLEES.

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Aims: Determine whether depot naltrexone is safe and effective to prevent relapse in parolees with opioid use disorder. All were volunteers, not referred by parole officers. Effectiveness was evaluated by randomly assigning parolees to 6 monthly naltrexone injections or treatment as usual (TAU) without medication.
Methods: All patients met DSM-IV criteria for opioid dependence. 308 parolees were randomized and 290 are now eligible for 6 month follow up. The naltrexone group received 6 monthly injections of 380 mg and a monthly visit with a nurse. The parolees randomized to TAU received help in joining a community counseling program. Outcomes were measured by urine tests and self-report.
Results: Retention rates in treatment at 27, 52, and 78 weeks were 64%, 58% and 54% for the TAU group and 66%, 54% and 52% for the naltrexone group. Urine tests were examined at 27, 52 and 78 weeks and with pooled data from all 5 sites, there were significantly fewer opioid positive urines in the naltrexone group ($p<.0001$ for the pooled analysis). The rate of positive opioids for TAU was 3.36 times higher than that for naltrexone. No significant difference was found for other drugs. There were 2 opioid overdoses in the TAU group and none in the naltrexone group. There were 4 deaths from all causes in the TAU group and 2 deaths in the naltrexone group un related to medication.
Conclusions: A monthly injection of depot naltrexone significantly reduced opioid relapse in parolees. Six month retention was similar in the two groups. Serious adverse events including opioid overdose occurred less often in the group receiving naltrexone (18 naltrexone v. 43 for TAU). In this interim analysis, depot naltrexone was found to be both safe and effective in reducing the rate of relapse to opioid use.
Financial Support: This research was supported by collaborative RO-1 grants to the 5 sites involved. The extended release naltrexone in the form of Vivitrol was supplied by Alkermes Inc.

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A NEEDS COMPARISON OF JUSTICE-INVOLVED IRAQ/AFGHANISTAN VETERANS TO OTHER SERVICE ERAS.

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Aims: To compare the service needs of veterans who served in Operations Enduring Freedom and Iraqi Freedom (OEF/OIF) versus other eras upon entry to a jail diversion program.
Methods: Ninety veterans enrolled in MISSION DIRECT-VET, a jail diversion program for justice-involved veterans with co-occurring disorders in four Massachusetts courts. Veterans completed the ASI-Lite, BASIS 24, PCL, and NOMS.
Results: Nearly 60% of veterans served in OEF/OIF (58%) versus other eras (42%). The average age of OEF/OIF veterans was 31 compared to 51 among non-OEF/OIF veterans ($p < 0.01$). Veterans were first booked, arrested, and taken into custody at age 22 in both groups. Veterans who served in the OEF/OIF conflicts were more likely to have served in a combat zone compared to non-OEF/OIF veterans (78.8% vs. 28.9; $p < .01$). Despite greater combat exposure, OEF/OIF veterans scored similarly on the BASIS 24 and PCL-C. However, OEF/OIF veterans were more likely to cite that their military service contributed to their medical ($p = 0.01$) and mental health or emotional problems ($p< 0.05$) compared to the non-OEF/OIF group. The average age of first contact with mental health services was lower among OEF/OIF veterans ($M = 20.4$, $SD = 7.7$) compared to non-OEF/OIF veterans ($M = 31.5$, $SD = 11.1$; $p < 0.01$). OEF/OIF veterans reported earlier contact with substance abuse services (24 years old) compared to age 30 for non-OEF/OIF veterans ($p < 0.01$). However, the two groups did not differ in their use of cocaine and alcohol in the past month.
Conclusions: Findings suggest that veterans with criminal justice issues who served in OEF/OIF have different programmatic needs compared to those who have served in other eras. The current data highlights information key for tailoring treatments for returning justice-involved veterans.
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NEIGHBORHOOD DISORDER, HIV TREATMENT ACCESS AND ARV DIVERSION: A MEDIATION STUDY OF DRUG-INVOLVED HIV POSITIVE INDIVIDUALS IN SOUTH FLORIDA.

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Aims: Recent research has indicated the presence of an illicit market for HIV antiretroviral (ARV) medications in South Florida. We examine possible environmental contributors to ARV diversion among impoverished HIV+ substance abusers. In particular, this analysis focuses on the role of neighborhood disadvantage in impacting access to HIV treatment and subsequent ARV diversion.
Methods: Participants were at least 18 years old, confirmed HIV+, and had used cocaine, crack or heroin at least 12 times within the last 3 months. By design, approximately half of participants endorsed recent diversion of ARVs (n=251). 503 participants completed a one-time face to face structured interview using standardized assessments. Mediation models were tested that examined the effects of neighborhood disorder and HIV treatment access on ARV diversion.
Results: Significant correlations were found between neighborhood disorder and ARV diversion ($r=0.09$, $p<0.05$), neighborhood disorder and HIV treatment access ($r=-0.10$, $p<.03$), and HIV treatment access and ARV diversion ($r=-0.12$, $p<0.01$). During mediation analysis, the correlation of neighborhood disorder and diversion became non-significant, leading to the assumption of mediation through the indirect path of HIV treatment access. An increase in neighborhood disorder was associated with a decrease in HIV treatment access; while a reduction in HIV treatment access was correlated with ARV diversion.
Conclusions: ARV diversion is problematic for individuals' quality of life as well as for public health. Our analysis documented significant impact of environmental stressors on ARV diversion among drug-involved HIV+ individuals. Further examination of the role of the community-level influences on diversion behaviors appears warranted.
Financial Support: This research was supported by the National Institute on Drug Abuse (grant R01DA023157).

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BI-DIRECTIONAL EFFECTS OF PRESYNAPTIC AND POSTSYNAPTIC ADENOSINE A_{2A} RECEPTOR ANTAGONISM ON COCAINE SEEKING.

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Aims: Repeated cocaine administration produces perturbations in dopamine and glutamate neurotransmission that contribute to the reinstatement of extinguished cocaine seeking. Postsynaptic adenosine A_{2A} receptors co-localize with dopamine D_2 receptors in nucleus accumbens neurons, while presynaptic adenosine A_{2A} receptors co-localize with adenosine A_1 receptors on glutamate terminals. The synaptic localization of adenosine A_{2A} receptors represent targets for altering the dopamine and glutamate systems to effect the expression of behaviors associated with relapse. The goal of these studies was to determine the effects of presynaptic or postsynaptic adenosine A_{2A} receptor antagonism on the reinstatement of cocaine seeking.
Methods: Male Sprague-Dawley rats self-administered cocaine in 10 daily self-administration sessions on a fixed-ratio 1 schedule. Lever pressing was extinguished in 6 daily extinction sessions. We first tested whether presynaptic and postsynaptic A_{2A} receptor antagonism (SCH 442416 and KW 6002, respectively) was sufficient to reinstate cocaine seeking. We next tested the effects of SCH 442416 and KW 6002 on reinstatement to cocaine seeking induced by cocaine.
Results: Administration of the postsynaptic adenosine A_{2A} receptor antagonist dose-dependently reinstated cocaine seeking and facilitated reinstatement induced by 5 mg/kg cocaine, a dose that was alone insufficient to reinstate cocaine seeking. Administration of the presynaptic adenosine A_{2A} receptor antagonist did not induce cocaine seeking when administered alone, but impaired cocaine-induced reinstatement induced by 15 mg/kg cocaine.
Conclusions: These findings highlight the importance of synaptic locations of adenosine A_{2A} receptors in regulating cocaine seeking. Thus, antagonism of postsynaptic A_{2A} receptors facilitates cocaine seeking, perhaps by enabling D_2 receptor signaling. Antagonism of presynaptic A_{2A} receptors, on the other hand, impairs cocaine seeking, perhaps by enabling adenosine A_1 receptor activation and inhibition of glutamate transmission.
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RELATIONSHIP BETWEEN ALEXITHYMIA AND DOPAMINE D2-TYPE RECEPTOR AVAILABILITY: METHAMPHETAMINE-DEPENDENT SUBJECTS DIFFER FROM HEALTHY CONTROLS.

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Aims: Alexithymia, a personality trait that refers to impairment of the ability to identify and describe feelings, is associated with substance use disorders. The goal of this study was to help clarify how brain function is related to alexithymia in individuals with substance use disorders and to evaluate the contribution of dopaminergic signaling to alexithymia.
Methods: Positron emission tomography with [18F]fallypride, a radiotracer with high affinity for dopamine D2-like receptors, was used to measure receptor availability, indexed by binding potential (BPND) in the anterior cingulate cortex (ACC) and the anterior insula (AI). Alexithymia was assessed using the 20-item Toronto Alexithymia Scale (TAS–20) and depression assessed with the Beck Depression Inventory (BDI). 24 methamphetamine (MA) users and 17 healthy control (HC) subjects participated.
Results: MA users had significantly higher TAS-20 scores than HC subjects, but the groups showed no significant differences in BPND. There was an interaction between BPND and group. Post-hoc analysis showed that BPND in ACC and AI was positively correlated with TAS-20 score in HC subjects (ACC: $p = 0.020$*; AI: $p = 0.024$*); however, BPND in ACC was negatively correlated with TAS-20 in MA users (ACC: $p = 0.019$*; AI: $p = 0.150$). *: $p < 0.05/2$
Conclusions: The findings indicate that dopaminergic signaling in ACC and AI contributes to alexithymia in healthy subjects, but the opposite is true in MA-dependent subjects. It suggests that these regions play an important role in emotion awareness, and that MA can change this relationship.
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CYP2A6 METABOLISM IN THE DEVELOPMENT OF NICOTINE DEPENDENCE IN ADOLESCENTS AND YOUNG ADULTS.

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Aims: To examine how variation in CYP2A6, the enzyme responsible for the majority of nicotine metabolism, influences nicotine dependence in a youth sample.
Methods: Since 2005, the Collaborative Study on the Genetics of Alcoholism (COGA) has recruited participants ages 12 to 22 from six US sites with assessments every two years. A subsample of 1,016 European ancestry individuals was genotyped for CYP2A6 variants to calculate a previously described metabolism metric, and more genotyping is underway. In this sample, 366 (36%) reported smoking at least 100 cigarettes and were considered smokers. Data were analyzed using the Statistical Analysis System, and logistic regression was used to model nicotine dependence with the Fagerstrom Test for Nicotine Dependence (FTND, score of 0-3 non-dependent smokers vs. ≥4 dependent smokers). Metabolizer status (slow metabolizers <0.85 by metric), gender, and last interview age were used as covariates.
Results: The sample was 40% female and 15% slow metabolizers with a mean first interview age of 17 years and last interview of 22 years. Among smokers, 51% of the normal metabolizers were FTND dependent (n=152/312), while 70% of the slow metabolizers were dependent (n=38/54). In the logistic regression model, being a slow metabolizer was associated with increased risk of FTND diagnosis after controlling for gender and last interview age (OR=2.3, p=0.009).
Conclusions: These preliminary findings suggest that CYP2A6 variation linked to slow metabolism is associated with increased nicotine dependence risk in adolescents and young adults. Some studies hypothesize that slow metabolism may increase sensitivity to nicotine in youth, causing increased progression to dependence. Future research will dissect the specific timing of smoking behaviors in this population.
Financial Support: This work was supported by U10AA008401 from the National Institute of Health (NIH). EO was supported by T32GM007200 and UL1TR000448, sub-award TL1TR000449, from the NIH.

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EVALUATING POTENTIAL MODERATORS OF EFFICACY FOR A SINGLE-SESSION COMPUTER-DELIVERED 5AS INTERVENTION FOR SMOKING IN PREGNANCY.

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Aims: In a previously published trial, a single-session, computer-delivered 5As/5Rs intervention (CD-5As) was associated with significant reductions in smoking (e.g., 24.5% 7-day point-prevalence abstinence at 10-week follow-up in the intervention group vs. 8.9% in the control group). The present study conducted secondary data analysis to evaluate potential moderators of intervention efficacy.
Methods: The original trial randomly assigned 107 low-income, primarily African-American pregnant women reporting smoking during pregnancy to intervention vs. control conditions and re-evaluated smoking 10 weeks later. The primary outcome in the original study, as well is in the current analyses, was 7-day point prevalence abstinence per self-report confirmed with carbon monoxide breath testing. Moderator analyses involved a series of binary logistic regressions, one for each of the four potential moderators of efficacy: smoking more than 10 cigarettes per day (26.2% of participants), nicotine dependence (positive score on the Fagerström Test of Nicotine Dependence; 52.7% of participants), mental illness (scoring above the published cutoff on the K6 screener; 23.6% of participants), or living with someone who smokes (61.8% of participants). These equations entered experimental condition (intervention vs. control) and moderator variables before entering a condition X moderator interaction term.
Results: None of the four interaction terms were significant, suggesting that the efficacy of the computerized 5As intervention was not moderated by any of the four measures studied.
Conclusions: In this sample, a computer-delivered brief 5As/5Rs intervention for smoking during pregnancy was equally likely to have a small to moderate effect on smoking, regardless of baseline smoking frequency, nicotine dependence, maternal mental illness, or presence of other smokers in the home.
Financial Support: DA021668

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EXISTENTIAL ANXIETY IN FIRST-TIME RECIPIENTS OF XR-NTX FOR OPIOID ADDICTION.

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Aims: Aims
Commitment to abstinence from opioids is difficult both to achieve and maintain for individuals recently addicted to opioid agonists like heroin or codeine. Extended-release naltrexone (XR-NTX) reduces the effort associated with achieving and maintaining abstinence, but how will patients who volunteer for the treatment respond to their first XR-NTX injection?
Methods: Methods
Medical & clinical study records of the first twenty (n=20) patients who received XR-NTX in Norway were reviewed for all symptoms of anxiety related to their first XR-NTX injection. A naloxone test excluded patient data caused by antagonist-induced withdrawal. We monitored anxiety as well as adherence to the two next XR-injections and any adverse events or subjective health complaints.
Results: Results
Preliminary findings as of abstract submission indicate that of n=20 patients, n=8 (40%) exhibited some type of anxiety reaction despite passing the naloxone test for physiological withdrawal. Less than half of these patients (n=3) had persistent anxiety- or health-related complaints and only two of them chose to refuse one of the following two injections.
Conclusions: Conclusion
Extended-release naltrexone may increase anxiety in patients short-term. This type of anxiety is not pathological, but related to the patient's perceived effectiveness of opioid antagonism in helping them achieve abstinence.
Financial Support: The Norwegian Research Council,The Norwegian Centre for Addiction Research and participating hospitals

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PERSONALITY TRAITS AND SEX UNDER THE INFLUENCE OF ALCOHOL DURING ADOLESCENCE.

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Aims: Alcohol use is one of the main factors associated with sexual risk. There is evidence that adolescents who have sex under the influence of alcohol (SUIA) tend to use condoms lesser. However, little is known about the factors that may predispose one to engage in having SUIA, as personality characteristics. This study examines the proportion of adolescents who have SUIA and analyzes the relationship between personality and engaging in SUIA during adolescence.
Methods: Participating were 1,458 student-adolescents from 18 high schools located in the north, south, east, and southeast of Spain. Comprising the sample were 738 males (50.6%) and 720 females (49.4%), whose average age was 14.91 (SD = 0.80; range: 14-16). The Spanish adaptation of the 16PF-IPIP Personality Inventory was applied to assess the following personality facets: warmth, emotional stability, gregariousness, agreeableness, sensitivity, trust, openness, sociability, perfectionism, and calm. Sexual behaviors were evaluated using a self-report measure. Only the participants who reported having had vaginal, oral and/or anal sex at least once were selected for the analysis (n=479). Of the sexually experienced participants, 47% (224/479) reported having had SUIA.
Results: Multiple binary logistic regression revealed greater risk of engaging in SUIA for adolescents with low score of warmth (OR = 0.93 [0.88-.97]) and high scores on confidence (OR = 1.06 [1.02-1.22]) and openness (OR = 0.91 [0.87-0.96]) ($\chi 2$ (10) = 30.29; p = 0.001).
Conclusions: Being more distant, impersonal, confident, adaptable and open-minded were related to engaging in SUIA. Almost half of the sexually experienced Spanish adolescents have mixed sex and alcohol. Identifying personality factors related to SUIA contribute toward detecting sexual risk profiles during adolescence and to designing more specific preventive strategies that take dispositional variables into account to achieve their goals.
Financial Support: Foundation for Research and Prevention in Spain (Ref. FIPSE 360971/10) and Vali+D program of the Culture, Education, and Science Department, Valencian Community Government (Ref. ACIF/2012/132).

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THE SIZE OF AFRICAN-AMERICAN FEMALE'S HEALTH NETWORKS: THE ROLE OF DRUG AND CRIMINAL HISTORIES.

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Aims: Research suggests that African American women have close relationships and there has been a surge in examining how social networks predict health behaviors. However, there is limited health network outcome research. This study hypothesizes that African American women with more substantial drug and criminal histories have smaller health networks.
Methods: Using data from the Black Women in the Study of Epidemics (B-WISE, n=344), the demographic, drug use, and criminal involvement variables significantly correlated with health network size were included in a negative binomial regression model.
Results: The average participant was single, 35 years old, and had a high school degree. The number of health network members ranged from 0 to 7, with 24% having no health network members (x=1.37, S.D.=1.14). Women who were involved with the criminal justice system at recruitment, had ever been arrested for a property crime, reported using alcohol multiple times per day, and screened positive for drug use had significantly smaller health networks at follow-up. In the multivariate model, African American women who were recruited from prison, as opposed to the community (IRR=.76, 95% CI: .58, .98), and screened positive for drugs (IRR=.88; 95% C.I.: .66, .97) had significantly smaller health networks.
Conclusions: Both drug use and incarceration history predicted African American women's networks and it's concerning that almost one-quarter of women had no one to talk to about their health. Having a small health network could negatively impact health outcomes, decrease the use of needed services (e.g., substance abuse and infectious disease treatment), and result in increased expenditures on medical services (e.g., more ER visits). Future research should examine the characteristics of African American women's health networks and their relationship with health behaviors and service utilization.
Financial Support: This research is funded by NIDA (R01-DA022967 & K02-DA35116, PI: Oser).

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COMPREHENSIVE WOMEN-CENTERED TREATMENT FOR SUBSTANCE USE DISORDERS IN THE REPUBLIC OF GEORGIA: CURRENT STATUS AND FUTURE DIRECTIONS.

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Aims: The present paper examines the current status of women-centered substance use disorder treatment in Georgia.
Conclusions: Four major issues are identified that adversely impact the delivery of effective services for women with substance use disorders: Sociocultural Issues; Policy Issues; Programmatic/Structural Issues; and Personal/Interpersonal Issues. These four issues are seen to form a complex, dynamic system that serves to maintain the current ineffective service delivery system and suppresses movement toward an effective service delivery for this highly marginalized and at-risk population. How these issues, and their interplay, present continuing barriers to the development and implementation of effective treatment for this population are outlined and discussed. In order to overcome these barriers, solutions must be sought in four areas: Public health campaigns; Development and implementation of comprehensive women-specific confidential treatment models; Policy reform; and Empowering women. Specific goals in each of these areas that would achieve a positive impact on various aspects of the functioning of the current service delivery system for women with substance use disorders are suggested. Simultaneously seeking solutions in all four of these areas may improve the service delivery system and benefits women with substance use disorders.
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PERCEIVED RISK OF REGULAR CIGARETTE SMOKING AND MARIJUANA USE IN THE U.S, 2002-2012.

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Aims: To explore changes in perceived risk of regular cigarette smoking and regular marijuana use in the United States over a 10-year period, and identify characteristics associated with perceived risk of use.
Methods: Data was obtained from the 2002 (N=54,079) and 2012 (N=55,268) NSDUH public use data files. Descriptive statistics and logistic regression analyses were used to describe the associations of socio-demographic and substance use characteristics with perceived great risk of regular use.
Results: Perceived great risk of regular cigarette smoking was reported in 2002 and 2012 by 71.2% and 71.7%, respectively (p=0.35). Decreased prevalence of perceived great risk of smoking between 2002-2012 was associated with: being previously or never married, past year alcohol/drug use, drug or alcohol abuse/dependence, past-year smoking, and nicotine dependence Increased prevalence of perceived great risk of smoking between 2002-2012 was associated with: females, older adults, Black race or Hispanic ethnicity, high school education or greater, higher income, and lifetime history of smoking. Perceived great risk of regular marijuana use was reported in 2002 and 2012 by 51.3% and 40.3%, respectively (p<0.001). Most characteristics were associated with decreased perceived great risk of regular marijuana use between 2002-2012; exceptions included respondents who were female, aged over 35, and non-White.
Conclusions: The overall prevalence of perceived great risk of regular cigarette use remained stable between 2002-2012, while the prevalence of perceived great risk of regular marijuana use decreased significantly. The odds of perceived great risk for each substance varied by population subgroup.
Financial Support: This work was supported by: T32 DA007209 (Pacek), R01 HD060072 (Martins) and T32 DA007292 (Mauro).

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MULTIMODAL IMAGING REVEALS ALTERED FUNCTIONAL AND STRUCTURAL CONNECTIVITY OF AFFECTIVE PROCESSING IN ALCOHOL DEPENDENCE.

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Aims: Alcohol dependence (AD) is associated with aberrant affective processing (AP) and changes in frontolimbic regions underlying AP. The current study aimed to characterize functional connectivity (fcMRI) of brain regions underlying AP in individuals with AD and healthy controls and relate fcMRI to white matter integrity.
Methods: Fourteen abstinent individuals with AD and 14 controls were included in this IRB-approved study. The facial AP task included fearful and happy expressions. Anatomical, functional, and diffusion tensor imaging data were collected. A psychophysiological interaction analysis was conducted for fearful and happy faces. In the AD group, functional anisotropy (FA) was calculated to measure white matter integrity. Independent samples t-tests were computed in AFNI to determine fcMRI cluster groups differences and follow up regression analyses were conducted including covariates.
Results: Fearful faces analyses revealed reduced fcMRI compared with controls between left amygdala and bilateral precuneus, right middle frontal, left postcentral, right lingual, bilateral fusiform, right middle temporal, right superior frontal, and right angular regions. Happy faces analyses showed reduced AD fcMRI with the left amygdala and right paracentral area. Increased white matter integrity (FA) predicted increased and decreased fcMRI during fearful faces One increased FA tract predicted increased fcMRI during happy faces.
Conclusions: Aberrant neural networks may relate to AD and structural markers may be one mechanism for observed differences in AP. Results also suggest that inhibitory networks may be related to structural variability in AD.
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CHANGE IN ADDICTION TREATMENT STAFF AND CLIENT SMOKING FOLLOWING A STATEWIDE SMOKING BAN.

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Aims: This study assessed smoking behavior, and smoking-related attitudes and services, in 8 New York addiction treatment programs before a statewide smoking ban was implemented (2008), 1 year after implementation (2009) and 5 years after implementation (2013).
Methods: A random sample of 10 New York addiction treatment programs was selected initially, however by 2013 only 8 programs remained in the sample. Data reported here refer to 8 programs with data available at all time points (2008, 2009, 2013). At each data wave, all staff and a convenience sample of clients in each program were surveyed concerning tobacco-related knowledge, attitudes, and practices (used by staff) or services (received by clients). Across all programs, staff sample sizes were n=218 (2008), n=218 (2009) and n=176 (2013). Client sample sizes were 329, 241 and 253, respectively by time.
Results: Staff smoking prevalence decreased from 34.4% in 2008 to 22.9% in 2013 (p=0.036), while client smoking prevalence remained stable (68.6% in 2008 versus 67.0% in 2013, p=0.022). Among clients who smoked, however, mean number of cigarettes per day (CPD) decreased from (15.0, SD=11.68) in 2008 to (10.6, SD=7.44) in 2013 (p<0.001). Tobacco-related attitudes and services reported by clients varied by program type. In methadone treatment programs, attitudes and services increased linearly over time. In residential programs, client attitudes and services decreased initially (2008-2009) but rebounded by 2013.
Conclusions: This cross-sectional design does not permit causal interpretation. However, we observed a significant decrease in staff smoking (34% to 22%), while the comparable change in New York State general population smoking was roughly 18% to 16%. Although clients reported a high prevalence of smoking at all time points, their mean CPD decreased, reflecting similar changes in the general population. Our findings also indicate that type of treatment program may be an important consideration as additional states implement tobacco policies in their addiction treatment systems.
Financial Support: NIDA P50DA009253

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ADHERENCE MONITORING FOR SUBSTANCE ABUSE CLINICAL TRIALS.

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Aims: During clinical trials, accurate measurement of adherence to experimental medication can decrease inappropriate rejection of potentially effective pharmacotherapies for stimulant addiction. We performed feasibility testing of a cellular phone-based adherence monitoring system and a confirmatory biomarker, riboflavin.
Methods: Eight subjects received iPhones with our capsule photo application and five 30 mg riboflavin capsules. Urine riboflavin concentrations were assessed at baseline. Each day, prompted by the application, subjects photographed a capsule in the palm of their hand using the application before ingesting the capsule. Urine samples were collected at 1, 2, 3, 4, and 6 hours after dosing on day 1, 2, 3, 4, and 5, respectively. Urine riboflavin concentrations were assessed using a commercial fluorometer and our low-cost, bench top fluorometer prototype. Results of both fluorometer readings were compared. Subjects rated the usability of the overall system on visual analogue scale (VAS).
Results: Our automated image recognition algorithm was 100% sensitive and specific in recognizing capsule photos. Capsule photos indicated that all doses were taken; urine riboflavin concentrations per both of the fluorometers were elevated following each dose. All urine riboflavin levels between 2 to 4 hours post-dose exceeded 1,000 ng/ml. On a scale of 0-100, average VAS scores for ease of use, simplicity, and likelihood of use of the system if available were 90, 91 and 82 respectively.
Conclusions: Adherence can be accurately assessed with our capsule photo application and fluorometer prototype. A cutoff urine riboflavin concentration of 1000 ng/ml between 2 to 4 hours after dose can be used to confirm adherence. Our adherence monitoring system was well accepted by the subjects. Next, we will develop a mobile adherence monitoring system that uses cell phone to obtain dosing data in real time combined with a Bluetooth enabled low-cost mobile fluorometer to measure urine riboflavin concentration in the field.
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HUMAN PHARMACOLOGY OF MEPHEDRONE: A DOSE-FINDING PILOT STUDY.

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Aims: Mephedrone is a synthetic cathinone included in the "Novel Psychoactive Substances" group. European epidemiological data showed a high prevalence of use. There are not experimental data in humans of the pharmacological effects of mephedrone. Objective was to obtain preliminary data on the effects of mephedrone and doses for future investigations.
Methods: Nine healthy male, recreational users of psychostimulants, participated as outpatients in three different experimental sessions, in which one of the substances was administered each day. They received single oral doses of mephedrone (n= 3, 50 mg, 100 mg and placebo; n=3, 150 mg, 200 mg and placebo; n=3, 150 mg, 200 mg and MDMA 100 mg). Drugs were administered double-blind, and randomised (lower doses were allocated before higher doses for safety reasons in case of 150 mg and 200 mg). Study variables included: vital signs (blood pressure, heart rate, temperature, pupil diameter), subjective effects (visual analog scales-VAS, ARCI-49 item short form, VESSPA questionnaire), and blood and urine samples for pharmacokinetics.
Results: Mephedrone produced effects at 150 and 200 mg, with dose-related increases of blood pressure, heart rate and pupil diameter (but not temperature). Mephedrone produced more intense effects than MDMA. Mephedrone induced pleasurable effects (ARCI-MBG, VAS "good effects", VAS "liking"), and mild changes in perceptions but not hallucinations.
Conclusions: Mephedrone produces dose-related effects in vital parameters and pleasurable subjective effects. Its pharmacologic profile is similar to MDMA and other psychostimulants.
Financial Support: Supported by grants from Instituto de Salud Carlos III (ISCIII, FIS-FEDER, FIS PI11/0196), ISCIII-Red de Trastornos Adictivos (RTA RD12/0028/0009). Clara Perez-Maña is a Rio Hortega fellowship (ISCIII, CM12/00085). Esther Papaseit is a Jordi Gras (PSMAR, 2013) and a Rio Hortega fellowship (ISCIII, CM12/00016, 2014).

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ROLE OF THE ENDOGENOUS CANNABINOID SYSTEM IN FEAR CIRCUITRY: TRANSLATIONAL FINDINGS AND CLINICAL IMPLICATIONS FOR POST-TRAUMATIC STRESS DISORDER.

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Aims: A decade of research has examined the role of endocannabinoid (eCB) receptors in brain circuits that exhibit dysfunction in individuals with post-traumatic stress disorder (PTSD). Findings are primarily from animal research that models distinct PTSD symptoms, such as stressful reactivity to cues that are no longer threatening, and from a few recent studies with healthy human participants. On this basis, and in the context of a political shift toward decriminalization of marijuana, some have suggested that cannabis may have therapeutic value in the treatment of PTSD. This critical review examines the evidence along two questions: (1) What neurophysiological mechanisms underlie the eCB system's role in fear extinction? (2) What are the potential risks and benefits of a therapeutic approach targeting the eCB system in individuals with PTSD?
Conclusions: Animal research provides strong evidence of the eCB system's involvement in fear extinction learning and an increasing understanding of its role in the hippocampus, amygdala, and prefrontal cortex—all areas of impaired functioning in PTSD. Disruption of the eCB system via genetic or pharmacological manipulations impairs fear extinction. In most cases, acute enhancement of the eCB system via administration of cannabinoid agonists or eCB breakdown inhibitors strengthens fear extinction learning. However, chronic administration of cannabinoid agonists impairs fear extinction, which highlights a potential risk of repeated use. Although promising, the translational value of these findings is limited by the type of interventions that are feasible in humans, the paucity of research, and the inconsistency of results in studies with non-disordered, cannabis-naive human subjects. There is evidence of dysfunctional signaling in the eCB system of individuals with PTSD, but further research is necessary to determine if they would benefit from treatment with cannabinoids, with cautious attention to prevalence of marijuana use among this population.
Financial Support: N/A

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THE ASSOCIATION BETWEEN BENZODIAZEPINE PRESCRIPTION AND ABERRANT DRUG BEHAVIORS IN PRIMARY CARE PATIENTS RECEIVING CHRONIC OPIOID THERAPY.

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Aims: Benzodiazepine (BZD) use in the setting of opioid therapy for chronic pain has been associated with an increased risk of overdose, but little is known about its association with aberrant drug behaviors. We aimed to examine the association between BZD prescription and aberrant drug behaviors in patients receiving chronic opioid therapy.
Methods: This was a retrospective cohort study using electronic medical record data on 847 patients with ≥ one visit to one of three primary care clinics between 9/1/11 and 8/31/12. All patients received ≥ three opioid prescriptions written ≥ 21 days apart within six months, and ≥ one urine drug screen during the study period. BZD exposure was determined by BZD prescription. A Cox proportional hazards model estimated the risk of a second early opioid refill, defined by an opioid prescription written 7-25 days after the previous prescription for the same drug, as a function of time-varying BZD exposure. A logistic regression model examined the relationship between BZD prescription and a positive urine test for cocaine. Models were adjusted for demographics, mental and substance use disorder diagnoses.
Results: Twenty-three percent (n=196) of patients received ≥ one BZD prescription during the study period. 22% (n=183) of patients had ≥ two early opioid refills and 9% (n=74) had ≥ one positive urine drug tests for cocaine. Receipt of BZD prescription was associated with an increased hazard of having ≥ two early opioid refills, adjusted hazard ratio (HR)=1.54 (95%CI, 1.09-2.18); but was not associated with increased odds for a positive cocaine test, adjusted odds ratio=1.07 (95%CI, 0.55-2.23).
Conclusions: Among primary care patients receiving chronic opioid therapy, BZD prescription was associated with ≥ two early opioid refills but not with cocaine use. Because alternative therapies exist for the primary indications for BZD prescription, further research should better elucidate the risks and benefits of prescribing BZDs to patients receiving chronic opioid therapy.
Financial Support: R01DA034252-01, R25DA033211

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EXPLORING THE EFFECTS OF ALCOHOL AND MARIJUANA USE ON EXPERIENCE OF TEEN DATING VIOLENCE AMONG HIGH SCHOOL STUDENTS IN MARYLAND.

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Aims: (1) To examine the association between marijuana and alcohol use and experience of teen dating violence (TDV), (2) to identify subtypes of alcohol and marijuana use, and (3) to examine the association between exposure to TDV and the alcohol and marijuana use classes among high school students.
Methods: Data come from 27,758 high school students participating in the Spring 2013 Maryland Safe and Supportive Schools Climate Survey. Alcohol and marijuana use was measured using two items assessing past 30-day use (0 days/1 or more days). The outcome, TDV, comes from two items assessing physical TDV and psychological TDV in the past 12 months (combined; experience any TDV/no TDV). Multilevel modeling (MLM) analysis was used to control for clustering of students within classrooms and schools. Individual-level factors examined include alcohol and marijuana use, age, sex, race; school-level factors examined include percent minority, percent suspension, and enrollment.
Results: Results indicate that 33% of the students reported recent alcohol use and 21% reported recent marijuana use. About 14% of students reported being hit, slapped, or physically hurt and/or threatened, degraded, or intimated by someone they were dating in the past year. The MLM revealed that students who reported using alcohol (β=0.64;p<.001) and students who reported using marijuana (β=0.67;p<.001) were at greater risk of experiencing TDV compared to students who did not report recent use of alcohol or marijuana. Latent class analysis will be used to address aim 2 and latent class regression will be used to address aim 3.
Conclusions: Preliminary findings suggest that alcohol and marijuana use may need to be addressed in TDV prevention or intervention programs.
Financial Support: This work was supported by the U.S. Department of Education's Safe and Supportive Schools Initiative and a NIDA T32 Training Grant (3T32DA007292-21).

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BEYOND AN ADOLESCENT'S FIRST OCCASION OF USING PRESCRIPTION PAIN RELIEVERS EXTRA-MEDICALLY: ASSOCIATIONS WITH SEX AND WITH ALCOHOL INVOLVEMENT.

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Aims: This is a study of adolescents engaged in extra-medical use of prescription pain relievers 'to get high' and for other reasons (EMPPR; mainly opioids), and their risk of becoming opioid dependent. Using nationally representative samples of newly incident EMPPR users assessed before age 21 years, we estimate male-female differences and test a theory-based hypothesis that alcohol dependence (AD) might accelerate progression from the 1st EMPPR occasion toward more serious opioids involvement within a span of 24 months after the 1st occasion of use.
Methods: Methods: Data are from U.S. National Surveys on Drug Use & Health (SDA, 2002-2012), with n=23,301 adolescent newly incident EMPPR users (age <21 years), identified via IRB-approved computerized self-interviews, which also assessed alcohol involvement, including DSM-IV alcohol AD. Weighted estimates with Taylor series variances are reported, based on zero-inflated Poisson (ZIP) regression models for complex data.
Results: ZIP estimates for adolescents point toward a modest but not statistically significant female excess in the conditional rate of EMPPR use after the 1st occasion of EMPPR use (p>0.05), with no male-female difference in the odds of EMPPR persistence beyond the 1st occasion (p>0.05). As for recently active AD, the estimates point toward a possible independent effect of adolescent-onset AD as a determinant of EMPPR persistence beyond the 1st occasion of EMPPR use (p<0.05), but no AD effect on the EMPPR rate if use persists (p>0.05).
Conclusions: Seedall & Anthony (2013) recently substantiated over-representation of girls among newly incident adolescent EMPPR opioid users. Extending that research, we did not find that adolescent girls have an excess rate of EMPPR use, once such use has progressed beyond the 1st trial occasion. However, adolescent-onset AD may accelerate the rate of progression of EMPPR use, although it does not appear to affect the probability of transitioning beyond the 1st occasion of EMPPR use.
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COLLEGE STUDENT OPINIONS ABOUT THE USE OF NON-MEDICAL PRESCRIPTION DRUGS.

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Aims: The use of NMPDs has risen among college students over the past 20 years. The aims of the study were to determine college student perceptions of: 1) the common types of NMPDs being used; 2) the reasons for use of NMPDs; and 3) the positive and negative consequences associated with NMPD use.
Methods: We conducted 8 focus group discussions with 61 students, who reported current NMPD use (i.e., past 3 months). The average age of the participants was 20 (SD = 1.6). The majority were male (64%), Caucasian (80%), and not Hispanic (81%). Nearly half (49%) were freshman or sophomores, and 46% lived on-campus.
Results: These students reported using several NMPDs (Median = 2, Mode = 3), and an average of 2.4 (SD = 1.2) other illicit drugs. Students reported stimulants, benzodiazepines, and opioids as the three most popular NMPDs used by college students. They indicated that stimulants were the most popular, least expensive, and easiest to obtain on campus, followed by benzodiazepines. Opioids were less popular, more dangerous because of their addiction potential, more difficult to find on campus, and far more expensive. They indicated primarily utilitarian reasons for using stimulants. These included: studying, getting more done, organizing and improving grades. They rarely reported using stimulants to get high, but did indicate using stimulants to drink longer or larger amounts. Benzodiazepines were used to come down from other drugs (e.g., stimulant crash, bad LSD trip), mellow out, or in combination with alcohol (e.g., intentional black out, increase intoxication). Opioids were described primarily for recreational use and as the best feeling the individual had ever experienced. Students indicated both positive and negative consequences associated with each NMPD. However, when asked why they continued to use NMPDs, they indicated that the positives far outweighed the negatives.
Conclusions: This study suggests that among those students currently using NMPDs, polydrug use is common and combined use of alcohol and NMPDs is of substantial concern.
Financial Support: SUNY/RF Collaborative Fund Award to Kathleen A. Parks

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LATINOS' ACCESS TO ONLINE AND FORMAL MENTAL HEALTH SUPPORT.

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Aims: We investigated online mental health support (OMHS) and help-seeking of Latino citizens living in United States communities, and estimate associations linking OMHS with a selection of individual and community variables. In addition, we examined the extent to which unmet mental health treatment needs among adults might be associated with key variables (e.g., economic resources, health insurance).
Methods: This research report's estimates are based on 39,630 Latino adult National Surveys of Drug Use and Health (NSDUH) participants during 2004 through 2010. A multiple logistic regression model was then specified to estimate covariate-adjusted OMHS associations. Weighted proportions were estimated for each possible explanation for no receipt of mental health treatment services; these estimates were then stratified by the language version of the survey taken.
Results: Latino adults who chose the Spanish version of the assessment were less likely to seek online mental health social support (inverse odds ratio, OR = 0.2; $p < 0.001$). Second, as compared to Latino adults who did not finish high school, those who earned a high school diploma but did not attend college were similar in their OMHS use, whereas those who had attended at least some college were more likely to be OMHS users, irrespective of whether they had earned a college degree (OR = 3.5, 95% CI = 1.3, 9.5; $p = 0.02$).
With regards to not obtaining formal mental health services, approximately 40% (95% CI = 0.35, 045) of Latino adults with unmet mental health treatment needs cited not being able to afford the cost of treatment as a prohibitive factor. However, roughly 5% cited a lack of health coverage.
Conclusions: Based on current findings, poverty and contextual variables continue to play a role in the barriers to mental health treatment services for vulnerable Latino populations. For example, accessing services can become prohibitive due to high deductibles or wide coverage exclusions.
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PROTRACTED ABSTINENCE INFLUENCES THE 'TUG OF WAR' BETWEEN PLEASANT AND COCAINE-RELATED CUES IN ADDICTED INDIVIDUALS: EVIDENCE FROM A LONGITUDINAL ERP STUDY.

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Aims: Attention-bias towards drug-related stimuli and away from other pleasant affective cues is a hallmark of addiction. With protracted abstinence, however, treatment-seeking individuals with cocaine use disorders (tsCUD) show some recovery of emotional functioning, but it is unclear how such prolonged abstinence impacts such attention-bias. Therefore, the aim of this study was to investigate if the protracted abstinence in tsCUD can shift the attention-bias away from cocaine-related cues and towards pleasant cues.
Methods: Nineteen tsCUD and 8 controls participated in the study in which event-related potentials (ERPs) were acquired while the participants passively viewed pleasant, unpleasant, neutral and cocaine-related pictures at baseline and then again after 6-month of abstinence. The late positive potentials (LPP) component of the ERP was scored to index motivated attention to these stimuli.
Results: A mixed ANOVA yielded a significant session (baseline and follow-up) by picture contrast (pleasant, unpleasant, and drug; relative to neutral) by group (tsCUD and controls) interaction [$F(2,24)=5.39$, $p=0.012$], driven specifically by increased pleasant LPP in tsCUD [$t(18)=2.38$, $p=0.028$] at follow-up compared to baseline. Planned comparison between sessions also showed a significant decrease in response to drug relative to pleasant pictures [$t(18)=2.66$, $p=0.016$] at follow-up compared to baseline in tsCUD.
Conclusions: Together, results show that longer-term abstinence is associated with increased salience of pleasant stimuli and relatively decreased salience of drug stimuli. These findings are consequential as they highlight the utility of ERP components as biomarkers of drug-mediated attention-bias with a potential for increased clinical use (e.g., to track treatment course or efficacy).
Financial Support: This study was supported by grants from the National Institute on Drug Abuse (to MAP: 1F32GA033088; to SJM: 1F32DA030017; to RZG: 1R01DA023579).

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HOW DOES BINGE DRINKING AFFECT RISKY BEHAVIORS ON THE ROAD?

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Aims: Alcohol abuse can lead to engaging in risky behaviors. In the context of road safety, evidence points to an association between binge drinking and crashes as well as injury severity. The aim of this study is to compare the differences between three groups of drivers: a) binge drank in the last year, b) who drank but did not binge in the last year and c) drivers who did not drink in the last year - in relation to socio-demographic characteristics and risky behaviors.
Methods: A knowledge, attitude and perception (KAP) survey was conducted among drivers from two capital cities (Palmas and Teresina), representing the North and Northeast regions of Brazil. In October and November 2013, 1,556 face to face interviews were conducted (30.3% binge-drinking [BD], 26% no binge-drinking [NBD] and 43.7% no drinking [ND]); sampling was done by quotas, according to driver's sex and age. The variables were analyzed through chi-square test.
Results: Drivers who reported binge drinking are younger (BD: 34.6±10.5 years; NBD: 38.2±12.2 years; ND: 40.5±13.8 years, $p<0.001$) and mostly males (BD: 81.6%; NBD: 74.5%; ND: 61.3, $p<0.001$). In relation to risky behaviors, 41% of those who binge drink used a cell phone while driving compared to 34.2% NBD and 25.6% ND ($p<0.001$); 60% of binge drinkers reported being passengers to drivers who had been drinking as compared to 46.5% NBD and 30.4% ND ($p<0.001$). Also binge drinkers comprised a greater proportion of drivers who were involved in a road traffic crash after drinking in the last year (BD: 15.9%; NBD: 6.2% and 5.1%, $p<0.001$).
Conclusions: Our findings suggest that binge drinkers are more prone to other risky behaviors, which could translate to greater vulnerability to road traffic injury. This information may be of use to authorities in Palmas and Teresina. We suggest additional research be done to understand motives behind drinking and driving behaviors, particularly among binge drinkers.
Financial Support: This study is supported by Bloomberg Philanthropies.

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WITHDRAWN

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A QUALITY IMPROVEMENT INNOVATION TO ESTABLISH A PCMH TAILORED TO HOMELESS VETERANS WHO UTILIZE THE ED.

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Aims: Homeless veterans have high rates of medical, mental health, and substance use co-morbidities, and emergency department (ED) and inpatient service utilization. In 2013, VA established a homeless-oriented patient centered medical home national demonstration program, referred to as the Homeless Patient Aligned Care Team (HPACT). Unlike traditional PCMH models, the West Los Angeles VA Medical Center (WLA) HPACT employed a series of complex primary care management interventions tailored to homeless Veterans seeking care in the ED for low-acuity problems.
Methods: Development of the WLA HPACT was carried out in three phases – literature review, diagnosis, and implementation. In phase 1, we conducted a literature review of the factors contributing to homeless Veteran ED utilization patterns. In the diagnosis phase, we undertook a local needs assessment (conducted by informal stakeholder focus groups) to determine the organizational context for the WLA HPACT program and how to best evaluate HPACT's objective to reduce ED utilization rates for HPACT patients. The implementation phase employed a mixed-method progress-focused formative evaluation to examine patient characteristics, intervention processes, ED utilization patterns, staff perceptions and interventions to decrease ED visits.
Results: Findings suggest high prevalence of patients with substance abuse needs (73%), increased engagement in substance abuse treatment programs after being enrolled in the HPACT program for 6 months (26%), and reduction in ED visits at 6 months (mean reduction 3.2 visits).
Conclusions: The findings of this QI effort inform clinical and organization processes for the WLA HPACT that should be considered for on-going implementation. Recommendations for future implementation include complex care management interventions for patients with pain needs, substance abuse conditions, as well as modifications to organizational features of the program such as hours of operations, and substance use/mental health team composition.
Financial Support: Financial support was provided by VA.

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INFLUENCE OF SENSATION SEEKING ON D-AMPHETAMINE REINFORCEMENT.

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Aims: Abuse of psychomotor stimulants is a significant public health problem. While many individuals experiment with stimulants, there is marked variability in the subjective and behavioral response to these drugs, which may influence susceptibility to abuse. One characteristic associated with drug use is sensation seeking (SS). While studies have suggested an association between SS and vulnerability for stimulant abuse, the precise relationship between these variables remains unknown.
Methods: We conducted a NIDA-funded laboratory study in which 37 healthy adults received repeated opportunities to sample and choose between d-amphetamine (d-AMPH; 5, 10, 20 mg/70kg) or placebo. The Zuckerman Sensation Seeking Scale V was administered at intake, providing an opportunity to investigate the influence of Total SS, as well as each of the four subscales, on sensitivity to d-AMPH reinforcement. Logistic regression based on GEE models was used to investigate the association between SS and d-AMPH choice. We hypothesized that elevated SS would predict subsequent increased d-AMPH choice.
Results: Participants were 22.9 + 2.9 yrs old, 57% female and had 15.1 + 1.3 yrs of education. Among males, SS was a significant predictor of d-AMPH choice, with each one standard deviation increase in Thrill and Adventure Seeking, Experience Seeking, Disinhibition, and Total SS score associated with an estimated 2.0, 2.1, 1.7, 1.7-fold greater odds of choosing d-AMPH, respectively. The strongest relationship occurred at the 10mg dose. Among females, SS was not associated with d-AMPH choice.
Conclusions: These preliminary results suggest that, even among healthy adults, elevated SS may be associated with increased sensitivity to d-AMPH, particularly among males exposed to a moderate d-AMPH dose. Analyses on the association between SS and subjective response to d-AMPH will also be presented at the meeting. This study represents the first to investigate the influence of SS on d-AMPH reinforcement using a discrete-trial choice procedure with multiple d-AMPH doses and multiple exposures to each dose.
Financial Support: R03DA027480 & T32DA007242

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THE ROLE OF HUMAN PLACENTAL TRANSPORTERS IN THE EFFLUX OF BUPROPION.

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Aims: The function of human placental efflux transporters is the extrusion of their substrates from the feto-placental unit to the maternal circulation. The aim of this investigation was to identify the placental efflux transporters involved in the extrusion of bupropion.
Methods: The expression of efflux proteins in placental apical membranes was determined by Western blots. The ATP-dependent uptake of [3H]-bupropion and [3H]-estrone sulfate was determined using commercially available inside-out vesicles (IOV) prepared from Sf9 insect cells transfected with one of the following human efflux transporters; MRP1, MRP2, MRP3, BCRP and P-gp. Bupropion inhibition of the ATP-dependent uptake of the [3H]-estrone sulfate in over-expressed systems and in placental IOV was utilized to determine the interaction of bupropion with each transporter.
Results: Protein expression of the efflux transporters in human placental apical membranes accounted for approximately 20% of the total proteins and was as follows: MRP1≈MRP2<MRP3<P-gp< BCRP. The ATP-dependent uptake of [3H]-bupropion and [3H]-estrone sulfate by BCRP, MRP1, and MRP3 expressed vesicles was determined. In the presence of 60μM bupropion, the uptake of [3H]-estrone sulfate by BCRP expressed vesicles was inhibited by 90%. Similarly, MRP1 and MRP3 expressed vesicles were inhibited by 50% and 30%, respectively. In addition, 60μM of bupropion inhibited the ATP-dependent uptake of [3H]-estrone sulfate in placental IOV by 40%.
Conclusions: The data strongly suggest that the placental efflux transporters BCRP, MRP1 and MRP3 could be involved in regulating the maternal-to-fetal transfer of bupropion during pregnancy.
Financial Support: Supported by a NIDA grant RO1DA030998 to TN and GH

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EXPLORING BRAIN MORPHOLOGY IN POLY-STIMULANT ABUSE: SHAPE, VOLUME, AND SURFACE AREA ABNORMALITIES IN ECSTASY-COCAINE-AND METHAMPHETAMINE-PREFERRING INDIVIDUALS.

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Aims: Stimulant abuse is linked to brain structural abnormalities, and increasingly sophisticated neuroimaging analysis methods can capture differences in increasing detail. Here, we used novel segmentation and shape mapping algorithms for the first time to explore cortical and subcortical morphology in stimulant abuse.
Methods: Human subjects meeting DSM-IV criteria for current stimulant abuse/dependence (N=79, 27 female, age 29.4±9.0yrs) and healthy control (HC) subjects with no drug use history (N=81, 30 female, age 29.4±9.2yrs) completed high-resolution T1-weighted MRI scans. Images were analyzed using a novel multi-atlas label-fusion based methodology (MAGeT Brain) along with a local shape metric that estimates surface displacement while accounting for volume differences. Stimulant-abusing subjects were categorized as cocaine (COC; N=14), methamphetamine (METH; N=17), and Ecstasy-preferring (ECS; N=48), and compared to HC using ANOVAs (controlling for age/sex).
Results: Compared to HC, COC subjects showed lower surface area in fronto-temporal cortex (surviving 5% FDR correction on the right, 15% on the left), and in caudate/putamen (10% FDR both sides). METH subjects also showed caudate/putamen abnormalities (shape differences), consisting of inward displacement medially and outward displacement laterally (5% FDR on left, 20% on right), and similar displacements in thalamus and globus pallidus (5-15% FDR). ECS subjects only showed lower cortical thickness in left prefrontal cortex (10% FDR).
Conclusions: Different stimulant drugs have differential morphological signatures (in part perhaps reflecting use pattern differences), replicating and extending previous structural findings. Our analyses, which capture anatomical features not detectable by volume analysis alone, can provide novel insights into neurodevelopmental and neurodegenerative aspects of stimulant abuse.
Financial Support: Supported by NIH grants DA17301, DA25096.

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PSYCHIATRIC SYMPTOMS IN A SAMPLE OF YOUNG, SEXUAL MINORITY BRAZILIAN ECSTASY AND LSD USERS.

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Aims: To assess demographics and psychiatric symptomatology of young club drug users to compare findings between heterosexual and sexual minority participants; to identify correlations between sexual orientation and depression/anxiety symptoms in the year before data collection
Methods: Cross-sectional study using ethnographic mapping and targeted sampling. Face-to-face interviews conducted in electronic music events and festivals using an adapted and shortened version of the Global Appraisal of Individual Needs. Past year DSM-IV depression and anxiety symptomatology were collected. The sample comprised 240 men and women; 171 reported heterosexual orientation, and 69 reported sexual minority orientation. All participants had used ecstasy, LSD or both in the 90 days before the interview, and were out of treatment.
Results: Substance use in the past 90 days: there was a higher prevalence of cocaine use among sexual minority participants (69.6% vs 49.4%, p<0.007) compared to heterosexuals. The scores of severity of drug use were compared across individuals with/without depression and anxiety. Depressed individuals presented higher scores of severity of substance use (p <0.009). Multivariate regression analysis revealed a positive association between heterosexual orientation and not having significant depression symptoms. The prevalence of depression symptoms was 37% higher for sexual minority participants compared to heterosexuals (PR = 1.79, 95% CI: [1:03, 3:11].
Conclusions: Sexual minority drug users were at higher risk for psychiatric symptoms of depression than heterosexuals in this sample. Consistent with the literature on syndemics, this may be a reflection of societal prejudice, stigma, and discrimination that this group experiences.
Financial Support: Fogarty International Center; Grant 1R03TW007612; Fundo de Incentivo e Auxílio à Pesquisa (FIPE) from Hospital de Clinicas de Porto Alegre, Brazil (GPPG-HCPA – n°07-391)

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NURSES' SCREENING AND REFERRAL BEHAVIORS AND OPINIONS ABOUT BRIEF INTERVENTIONS BEFORE AND AFTER IMPLEMENTATION OF PROJECT ENGAGE.

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Aims: Project Engage (PE), implemented at Christiana Hospital in DE in 2013, is a brief intervention to engage non-trauma patients presenting with a variety of medical problems and found to have drug/alcohol problems in substance abuse treatment. Describe any changes in Emergency Department (ED) nurses' screening and referral behaviors and attitudes about the efficacy of brief engagement interventions subsequent to program implementation.
Methods: 37 nurses completed an online survey shortly before and 6 months after implementation. They also received a brief orientation to PE.
Results: Repeated measures t-tests revealed significant pre-post improvements in: screening for drug problems (t(35)=3.08, p=.004); referral to peer counselors for alcohol problems (t(23)=3.54, p=.002) and drug problems (t=(22)3.12, p=.005); and opinion of the effectiveness of brief interventions to help patients cut down/quit substances (t=(33)3.40, p=.002) and get into substance abuse treatment (t(32)=4.54, p=.000). There was no significantly significant increase in screening for alcohol problems, since those screening rates were high before PE's implementation.
Conclusions: Nurses' opinions and support are vital to program success. These data demonstrate that nurses' screening and referral behaviors and opinions on the effectiveness of brief engagement interventions may improve subsequent to program implementation.
Financial Support: Nursing Professional Excellence, CCHS; Anonymous donor, CCHS (PE); NIDA grants U10 DA-13043 (Woody, Pecoraro) and KO5 DA-17009 (Woody).

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HIGH RATES OF RELAPSE IN ADOLESCENT CRACK USERS AFTER INPATIENT CLINIC DISCHARGE.

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Aims: The aim of this study was to evaluate the trajectory of 88 teenage crack users referred for hospitalization and follow them up after discharge, checking for relapse and psychosocial aspects associated with treatment.
Methods: Cohort study (30 and 90days) of patient from a psychiatric hospital and a drug treatment clinic in Porto Alegre, Brazil, between 2011 and 2012. Data analysis on admission: the relationship among the Crack Use Relapse Scale (CURS) categories with relapse was performed to identify its prevalence ratio. Instruments: Semi-structured interview, conducted to evaluate the sociodemographic profile and describe the pattern of psychoactive substance use; CURS; Questionnaire Tracking Users to Crack; K-SADS-PL.
Results: First follow-up: 65.9% had already relapsed. Second follow-up: 86.4% of total sample had relapsed and half of the subjects had relapsed within 10 days after discharge. We observed that 34% were readmitted in public health settings and 36% had been involved in crime at the end of the 3 months follow-up.
Conclusions: This is one of the first studies that show the extremely high prevalence of early relapse in adolescent crack users after discharge, questioning the cost/benefit of inpatient treatment for this population. Moreover, these results corroborate studys which suggested, young psychostimulants users might need tailored Intensive Outpatient Treatment with contingency management and other behavioral strategies, in order to increase compliance and reduce drug or crime relapse, but this specific therapeutic modality is still scarce and must be developed in Brasil.
Financial Support: Brazilian Secretariat for Drug Policies (SENAD)

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INCENTIVIZING ADHERENCE TO PROLONGED EXPOSURE FOR PTSD: PRELIMINARY RESULTS.

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Aims: Postttraumatic stress disorder (PTSD) is a highly prevalent comorbid diagnosis in substance use disorder treatment. Unfortunately, patients rarely receive the most effective treatment for PTSD—Prolonged Exposure (PE)—due to concerns about increased drug use. Although there is scant evidence for increased drug use, most studies have demonstrated problems with very poor attendance to the therapy. In one study of an exposure-based treatment, patients attended a median of 5 of 13 scheduled therapy sessions and 0 exposure sessions (Mills et al., 2012). We hypothesized that providing voucher-based incentives for attendance to PE sessions would increase adherence and, by extension, result in good PTSD outcomes with no increase in drug use.
Methods: To date, 30 of 62 methadone-maintained participants have been enrolled, with 25 having finished treatment. Fourteen participants received PE alone (PE) and 11 received PE with incentive payments for attendance to sessions (PE+I). Voucher-based incentives begin at $30 per session, escalating by $10 to $60, with reset to $0 for a missed session (max payment $480). Most participants are women (88%), on average 35 years old (SD = 10), and racially and ethnically diverse (40% minority).
Results: PE+I participants attended a mean of 8.2 sessions (median = 9; SD = 3.4) while PE participants attended a mean of 1.6 sessions (median = 1; SD = 1.7; $p < .001$). PE+I participants were far more likely to have attended at least one exposure session (91% vs. 14%; $p < .001$). Forty-six percent of PE+I participants were treatment completers while no PE participants met criteria for treatment completion ($p < .001$).
Conclusions: More data will be available by presentation time on changes in PTSD symptoms, drug use, and drug treatment retention. These preliminary results, however, already demonstrate far better attendance to Prolonged Exposure for PTSD than previous studies, including more participation in the active portion of the treatment.
Financial Support: Supported by NIH R34DA032689.

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COMPARISON BETWEEN FORMER OPIATE ADDICTS ON METHADONE MAINTENANCE TREATMENT AND MEDICATION FREE FOR ≥10 YEARS.

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Aims: Opiate addiction is a chronic relapsing brain disease, which is best treated by MMT. Still, there are few (<10%) persons that succeed to live without medication. We compared sleep indices, chronic pain and cognitive status between two groups of former opiate addicts: current MMT patients and persons who succeeded ≥10 years to maintain medication free abstinence
Methods: Current MMT patients in treatment for ≥ 10 years, with negative urines for opiate, cocaine, benzodiazepine, cannabis, amphetamines for ≥3 months. Medication free abstinent persons (MF): former opiate addicts, with medication free abstinence for ≥ 10 years. Addiction indices, psychiatric disorders, sleep quality (PSQI), daily sleepiness (EPPS), Mini mental exam test (MMES) and Clock Drawing Test (CDT) were compared
Results: MMT (n=39) and MF (n=99) groups did not differ in age (53.5±7.8y), education years (10.1±2.9y), rates of sera-positive hepatitis C (48.7% vs. 33.7%, p=0.1) and HIV (5.1% vs. 2.0%, p=0.3). MMT patients had higher proportion of female (35.9% vs. 19.2%, p=0.05), of patients with any Axis I DSM-IV-TR psychiatric diagnosis (51.3% vs. 15.2%, p<0.0005), of chronic pain (48.7% vs. 26.2%, p=0.02), of poor sleep (PSQI>5) (64.1% vs. 38%, p=0.01) and of impaired cognitive state measured by MMES scored<27 (23.8% vs. 7.5%, p=0.01) and by CDT<3 (60.7% vs. 32.5%, p=0.01), but did not differ in rate of daily sleepiness (EPPS>7)(51.3% vs. 62.5%, p=0.3). Logistic regression characterized MMT patients as suffering more from DSM-IV-TR Axis I psychiatric diagnosis, chronic pain, and characterized as having poor sleep and worse cognitive state.
Conclusions: Treatment of chronic pain may improve sleep quality and cognitive state. Prevalence of DSM-IV-TR Axis I psychiatric disorders may differentiate between those who succeeded to manage protracted abstinence and those who did not succeed. Future studies, in particular genetic ones, are needed in order to better understand the differences between these two groups.
Financial Support: Adelson Family Foundation

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EXPLORING GENDER IN RESPONSE TO PROVOCATIVE STIMULI IN LIMBIC REGIONS OF INTEREST AMONG COCAINE USERS.

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Aims: An individual's neural response to natural rewards promotes survival and mental well-being. Although it is well established that non-drug using women generally have a higher neural response to provocative stimuli than men, and that cocaine using men typically have a blunted neural response to naturally arousing stimuli, less is known about the neural reactivity of cocaine using females to naturally arousing stimuli. The purpose of this study was to determine if the blunted neural response to naturally arousing cues previously observed in male cocaine users was also present in female cocaine users.
Methods: In this functional MRI experiment, non-treatment seeking cocaine dependent individuals (n=20, 50% female) and gender-matched controls (n=20, 50% female) viewed blocks of highly arousing positive, negative, and neutral images from a standardized database. For each individual the percent BOLD signal change (PSC) was calculated for a network of neural regions involved in limbic processing. These were compared across gender and drug use groups.
Results: Among men, there was no significant difference in the neural response to highly arousing positive or negative image between the cocaine users and controls. Among women, cocaine users had significantly lower neural activity than the controls for both positive images (i.e. ACC, ventral and dorsal medial prefrontal cortices) and negative images (i.e. ACC). Additionally, cocaine-dependent women had significantly less ACC activity than cocaine-dependent men when viewing positive images.
Conclusions: The results show that female cocaine users have a blunted neural response to naturally arousing stimuli relative to gender-matched controls and their cocaine-dependent male counterparts. These results establish a need for gender-specific treatment plans to target the emotional dysregulation in female cocaine users and tailor therapeutic techniques to increase emotional reactivity in this population.
Financial Support: R25DA020537, F32DA036329, K01DA027756

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CONCOMITANT ADRENAL HORMONAL STRESS RESPONSES ARE REQUIRED FOR COCAINE-INDUCED LOCOMOTOR SENSITIZATION.

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Aims: Cocaine-induced locomotor sensitization is a robust increase in locomotion to a standardized dose of cocaine. The associated neuronal changes that underlie increased behavioral sensitization involve addiction-related plasticity. Strong evidence suggests that the systemic stress response is involved in establishing addiction-related behaviors. We previously reported that the systemic adrenal response is required for escalation of addiction-related behaviors and that glucocorticoids in particular play a role in facilitating long term neural adaptions that result in these behaviors. Here we examine whether increased levels of the adrenal hormones, corticosterone (cort) and epinephrine (epi), either alone or in concert, are required for establishing locomotor sensitization to cocaine.
Methods: Male Sprague-Dawley rats underwent surgical adrenalectomy (ADX) with basal cort replacement and were administered cocaine for 10 days. On days 1 and 10 locomotor sensitization was tested by administration of 15 mg/kg, ip cocaine, while sensitization was induced on days 2-9 by administering a high dose of cocaine (30mg/kg, ip x 8 days). To test the role of the glucocorticoid receptor (GR) in induction of sensitization, the GR antagonist, RU 486 (12.5 mg/kg, sc) was administered prior to cocaine administration. To test whether replacement of the adrenal-secreted stress hormones would rescue sensitization in ADX rats, we replaced normal cort (2mg/kg) and/or epi (0.01mg/kg) during cocaine administration.
Results: The induction of sensitization was reduced in rats with ADX or pretreated with RU 486. In ADX rats, replacement using cort or epi alone did not recover locomotor sensitization but did rescue sensitization when co-administered.
Conclusions: These findings demonstrate that coordinated systemic stress signaling from the adrenal gland during cocaine administration is required for cocaine-induced locomotor sensitization and may play a role establishing addiction-related neuroplasticity with chronic cocaine use.
Financial Support: DA015758 to JRM and Diversity Supplement to DFP

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COMPARING SMOKING CESSATION INTERVENTIONS FOR PERSONS WITH SERIOUS MENTAL ILLNESS.

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Aims: This study compared two smoking cessation interventions for persons with persistent serious mental illness (PSMI) with a minimal intervention control.
Methods: PSMI (N = 180, 78% of referred) were recruited from a public agency. Participants smoked at least 10 cigarettes daily 3 years or more. Active interventions were contingent reinforcement (CR), and CR plus nicotine replacement via patch (CR+NRT) for 16 weeks. CR was escalating financial compensation for achieving and maintaining abstinence, as measured by breath CO. A longitudinal design was used with main outcome analyses conducted at baseline and weeks 20 and 36. Measures included: Smoking History/Status, Vitals, Salivary Cotinine (SC), CO, Brief Symptom Inventory, NRT Use, Interest in Quitting. Separate logistic regression models were conducted on SC and CO levels, with Intent-to-Treat analyses.
Results: At baseline, 48% reported intentions to quit smoking and 50% wanted to reduce. Breath CO showed that CR and CR+NRT participants had a higher quit rate than controls (58% v 18%; $\chi 2$ =12.84, p<.000). However, CO and self-report outcomes were discordant with SC outcomes, which yielded a non-significant difference between intervention and control groups (11.6% v. 10.7%; $\chi 2$ =0.15, p=.901) at weeks 20 and 36. Also, there was reduced smoking by SC levels at week 20; the CR and CR+NRT group results indicated light smoking, v the self-quit group (32%, 12%, 4%, respectively, p= 0.02). Importantly, there was no evidence of psychiatric exacerbation for any of the groups over time regardless of amount of smoking or diagnostic category.
Conclusions: This sample was very interested in quitting or reducing. Results suggest that smoking intervention efforts for PSMI should not be hampered by fears of decompensation. The data suggest that adherence to NRT should be reported in studies in this population; other forms of NRT could be explored. A reduction approach versus abstinence could be studied.
Financial Support: The Arizona Biomedical Research Commission (formerly the Arizona Disease Control Research Commission) Grant # 7014 & La Frontera Arizona.

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THE IMPACT OF EYE MOVEMENT DESENSITIZATION AND REPROCESSING AND SCHEMA THERAPY ON ADDICTION SEVERITY AMONG A SAMPLE OF FRENCH WOMEN SUFFERING FROM PTSD AND SUD.

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Aims: The purpose of the study is to examine the effects of eye movement desensitization and reprocessing (EMDR) associated with Schema Therapy (ST) on the improvement in symptoms of posttraumatic stress disorder (PTSD), attachment disorder (AD) and substance use disorder (SUD) among women in outpatient substance abuse treatment.
Hypothesis: PTSD and AD severity reductions with EMDR-ST focused on addictive memory were likely to be associated with substance use improvement.
Methods: This study investigated in the treatment of SUD among 7 women with SUD and PTSD comorbidity. We proposed a 3-phase-protocol therapy:
-a: 8 EMDR sessions focused on reprocessing traumatic memory; -b: 8 EMDR sessions (traumatic memory) associated with ST (traumatic attachment) and –c: 8 EMDR sessions (addictive memory) associated with ST.
We evaluated PTSD symptoms (PCL-S), Early Maladaptive Schemas-EMS (YSQ-S2) and addiction severity (ASI) before and after treatment (t-tests).
Results: The first phases of treatment protocol reduced PTSD symptoms (a and b) and EMS (b) but not the addiction severity (AS). AS and craving started significantly decreasing only after the last 8 additional sessions (EMDR-ST) focused on addictive memory (c).
Conclusions: In a previous study we showed that 6 women with SUD-PTSD and assigned to eight sessions of EMDR (traumatic memory) showed a significant reduction in PTSD symptoms but not in addiction symptoms compared to 6 control patients (treatment as usual). The present study suggests that reprocessing both traumatic and addiction memories using EMDR procedure associated with ST reduces not only PTSD and EMS but also AS. Results support importance of coping with PTSD symptoms and of providing integrative therapies for improving substance use outcomes especially in female patients because of the high frequency of stress-induced craving among women.
Financial Support: none

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WITHDRAWN

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PERCEPTIONS OF GENETIC TESTING AND GENOMIC MEDICINE AMONG URBAN DRUG USERS.

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Aims: The promise of genomic medicine is that individual-level genetic information can be used to optimize prevention and treatment interventions. Genetic testing (GT) has entered care for infection with human immunodeficiency virus (e.g., HLA B5701 testing) and hepatitis c virus (e.g., IL28B testing), and will soon do so for addiction. A paucity of data exists on how best to incorporate GT testing into healthcare for marginalized populations such as drug users (DUs), especially racial and ethnic minority DUs. We explored DUs perceptions of GT.
Methods: Six focus groups were conducted with active DUs recruited from syringe exchange programs and an HIV clinic between May 2012 and June 2012 in New York City. Individual interviews were conducted with 3 participants who reported previous GT.
Results: Of 34 participants, 44% female; 26% Black, 41% Hispanic, 33% White. 41% reported having HIV/AIDS, 6% reported having HCV, 6% reported HIV/HCV co-infection. Most had some awareness of GT, though experiences with prison and paternity testing. All welcomed GT if it could improve care, but most had concerns regarding confidentiality and implications for law enforcement. Many were dubious about race-based GT not understanding why efficacious treatments might not work for all groups; most expressed more comfort with GT based on individual consideration rather than testing based on race/ethnicity. GT-experienced peers were identified a source of trust in GT. Participants were generally more comfortable with GT when specifically asked permission and given a clear rationale, and with testing in medical care rather than in drug abuse treatment settings.
Conclusions: Participants had a general sense of the potential value of GT, yet concerns regarding confidentiality and discrimination may reduce testing willingness. Safeguards against these risks, peer support, and testing in medical settings based on individual factors and with clear rationales provided may be critical in efforts to promote acceptance of GT among drug users.
Financial Support: National Institute of Health grant P30 DA 011041

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LONG-ACCESS METHAMPHETAMINE SELF-ADMINISTRATION ALTERS REACTIVITY TO NOVEL CUES: IMPLICATIONS FOR CUE-INDUCED RELAPSE.

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Aims: Methamphetamine abuse is a growing problem in the United States, and research suggests that prolonged exposure to meth may lead to cognitive deficits. Rodent models of methamphetamine self-administration have revealed differences in animals given short periods of access to methamphetamine (SA: short access) versus those given longer periods of access to the drug (LA: long access). For instance, LA rats show deficits in novel object recognition, whereas SA rats do not. We were interested in how this particular deficit in novelty recognition would alter relapse in a situation where both novel cues and methamphetamine-associated cues are present. We hypothesized that SA rats would prefer novel cues compared to LA rats.
Methods: Sixteen male, Sprague-Dawley rats were trained to self-administer methamphetamine over 1 week in daily 1-hour sessions. They continued self-administering an additional 2 weeks under SA versus LA conditions (1-hr vs. 6-hr sessions). After 1 week of home-cage abstinence, rats were tested for cue-induced relapse. On this test, a novel lever + novel cue light was positioned on the wall opposite the meth lever + meth cue light. Responding was recorded on each lever for 1-hour. Methamphetamine was no longer available, but responding on the meth and novel levers resulted in presentation of their respective 15-second cue lights. The novel cue light differed from the meth cue light in shape and tactile properties, but its position relative to the novel lever and stimulus duration were identical to the meth lever + meth cue light.
Results: Results indicate that LA rats respond more on the meth lever (t-test, $p<0.01$), whereas SA rats respond equally on the meth lever and the novel lever (t-test, $p=0.35$).
Conclusions: This difference may reflect an increase in the salience of methamphetamine-associated cues after prolonged drug exposure, along with a relative diminution in the salience of novel cues. Additional studies are underway that attempt to reverse this pathology in the LA rats and restore the salience of novelty.
Financial Support: DA033049 to C.M.R.

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CARELESS AND OVERPROTECTIVE FATHERS ARE ASSOCIATED WITH ANTISOCIAL CRACK USERS.

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Aims: Several studies indicate that the perception of parental care received during childhood and adolescence may enhance or minimize risk for initiating use of illegal drugs and devepment of mental disorders, especially Antisocial Personality Disorder (ASPD). The goal of this study was to compare the perceived quality of parental bonding among crack users, with and without Antisocial Personality Disorder and assess the severity of illegal behavioral problems between the two groups.
Methods: Cross-sectional study of perceived quality of parental bonding among male crack users admitted for treatment in Porto Alegre, Brazil as measured by the Parental Bonding Instrument (PBI) Mother (n198) and Father (N173). The Addiction Severity Index (ASI-6) was used to assess the prevalence of violence and legal issue; psychiatric comorbidities were evaluated using the Mini International Neuropsychiatric Interview Plus (MINI-Plus).
Results: Antisocial behaviour (theft, robbery, burglary) was identified before age 18 (51.7%), and then, in adulthood, establishing ASPD (50.0%) respectively ($p<0.001$). The Poisson regression showed that subjects with ASPD perceived their fathers as having a 5% lower prevalence of the Care factor and a 5% higher prevalence of the Overprotection factor as compared with subjects without ASPD. Patients with ASPD were much more likely to be unmarried than those without ASPD (64.4% vs 17.8%; $p<0.001$).
Conclusions: The perception of a less caring but overprotective father figure may be a risk factor for the development of ASPD, use of crack, and difficulty in the ability to bond. We hypothesize that the lack of an appropriate male model of authority, an organizer of contingencies and parameters of reality, could hinder the development and structuring of the personality of men, leading to behavioural issues and crack use.
Financial Support: SENAD under grant #(GPPG-HCPA n.10/0002)

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SMARTPHONE-REPORTED STRESS AND DRUG EVENTS AND DAY-END PERCEIVED STRESS, HASSLES, AND MOOD IN METHADONE-MAINTAINED INDIVIDUALS.

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Aims: To determine relationships among drug use and stressful events and day-end reports of perceived stress and hassles.
Methods: Opioid-dependent methadone-maintained individuals in a 12-month natural-history study carried smartphones for up to 36 weeks to provide Ecological Momentary Assessment (EMA) data. They initiated event-contingent entries whenever they used drugs or experienced a stressful event, and completed a day-end assessment every night, including 5 items from the Perceived Stress Scale (PSS), 32 hassle items from the Hassles and Uplifts Scale (HS), and a brief mood assessment.
Results: Participants (n=102) reported 1016 stress events, of which 613 (60%) had corresponding day-end assessments, and 1171 drug-use events, of which 832 (71%) had corresponding day-end assessments. Compared to days on which no stress events were reported, stress-report days had higher day-end PSS scores (mean±SD, none 6.2±3.3 vs. stress 6.5±3.7, $p=0.04$) and higher day-end HS scores (mean±SD, none 2.2±3.6 vs. stress 3.6±4.5, $p<0.005$). Compared to days on which no drug use was reported, drug-use days had higher day-end PSS scores (mean±SD, none 6.1±3.4 vs. drug 7.3±3.2, $p<0.005$) and higher day-end HS scores (mean±SD, none 2.2±3.6 vs. drug 2.9±4.4, $p<0.005$). On days on which a stress event was reported, individuals more often rated their mood at day-end as angry/annoyed/afraid ($p<0.005$) and sad ($p=0.006$) and less often as content ($p<0.005$). On days on which drug use was reported, individuals more often rated their mood at day-end as sad ($p=0.005$) and less often as happy ($p=0.003$).
Conclusions: Using EMA to collect real-time in-the-field data, we found that both drug and stress events are associated with higher day-end perceived stress, hassles, and negative mood among opioid-dependent individuals in methadone maintenance. In addition to focusing on reducing drug use, addiction treatment should include education on stress, hassles, and mood management.
Financial Support: This research was supported by the National Institute on Drug Abuse-IRP, National Institutes of Health.

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DAILY MARIJUANA USE AND CRAVING IN THE ACADEMIC SETTING: A STUDY USING ECOLOGICAL MOMENTARY ASSESSMENT.

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Aims: Limited past research has examined the impact of marijuana use and craving on college students' academic motivation and performance. We speculate that marijuana craving may impact the cognitive focus of students, as well as their motivation for academic work. Furthermore, the social context in which marijuana is consumed may play an important role in academic success. Using ecological momentary assessment, we aimed to explore the relationship between marijuana craving, social context, and academic motivation in the moment.
Methods: Active college-student marijuana users (n = 57) were recruited and completed a baseline assessment and training on the two-week EMA protocol. Participants were texted nine questions, three times per day for two weeks. Academic motivation and craving were assessed on 1-10 scales (low to high), while social context focused on whether participants used marijuana alone or with others.
Results: The sample was 63% female, 79% Caucasian, and averaged 20.05 (SD = 2.60) years of age. Mean cumulative GPA was 2.86 (SD = .68; range from .80-4.00). Participants were heavy marijuana users, smoking two times per day on average (M = 2.50, SD = 2.37). HLM was used to assess the impact of social context on craving, adjusting for day of the week. Social context was significant ($p = 0.003$) with a positive association, suggesting that being with others was associated with higher levels of craving. Another HLM was fit to assess the impact of craving on academic motivation in the same EMA instance, adjusting for day of the week and time spent smoking and studying. This model showed that craving has a significantly negative association with academic motivation ($p = 0.02$).
Conclusions: Participants who smoked marijuana with others reported higher craving, suggesting that peer interaction could influence craving. Greater craving was associated with lower academic motivation in the same EMA instance. Future studies should examine whether marijuana craving and other social factors contribute to academic success.
Financial Support: This study was supported by an internal university provost award.

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NICOTINE AND STRESS: A ROLE FOR THE GLUTAMATE SYSTEM.

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Aims: The aim of the study is to investigate the glutamate reuptake system to determine if activation of glutamate transporter subtype 1 (GLT-1) by the β-lactam antibiotic ceftriaxone (CTX) affects the development and extinction of nicotine-induced conditioned place preference (CPP) in rats. In addition, the forced swim assay was used to examine the impacts of stress on nicotine-induced CPP.
Methods: The effect of ceftriaxone was tested in the rat CPP paradigm. Nicotine (0.4 mg/kg, subcutaneously) was administered daily for 4 consecutive days to induce CPP. CTX (200 mg/kg, intraperitoneally) was given in two different paradigms, one concurrently with nicotine to examine its impact on the development of CPP and one after the establishment of nicotine-induced CPP to examine its impact on the extinction of the preference. In a separate study, rats were subjected to a 15 min force swim session to induce stress at two different time points. The rats were exposed eighteen hours and one hour before the post-test. While the other rats were swimming, the control rats remained in their home cage.
Results: CTX did not significantly impact the development of nicotine-induced CPP but did accelerate the extinction of the CPP compared to vehicle-treated rats. Experiments revealed that nicotine preference was significantly enhanced by forced swim stress.
Conclusions: Taken together, these preclinical results suggest that the rewarding properties of nicotine are exacerbated by stress and disrupted by activation of cellular glutamate reuptake. These findings further suggest that CTX and GLT-1 activators should be studied as a potential therapeutic agent to treat nicotine addiction.
Financial Support: NIH/NIDA T32 DA007237

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NICOTINE DEPENDENCE AMONG DISTINCT SMOKING TYPOLOGIES.

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Aims: Questionnaires such as the Fagerström Test for Nicotine Dependence (FTND) and the Nicotine Dependence Syndrome Scale (NDSS) quantitatively estimate nicotine dependence and assist with determining therapy choice in tobacco cessation. The FTND yields a single score that indicates level of dependence) while the NDSS yields an overall score (OS) and scores on subscales that index constructs that contribute to dependence: drive (D), stereotypy (S), continuity (C), priority (P) and tolerance (T).
Methods: We report on the use of the NDSS to determine differences in OS or in various constructs of dependence among smokers who exclusively use Factory Made (FM, n=20), Personal Machine Made (PMM, n=23) or Roll Your Own cigarettes (RYO, n=34). In a second study, the NDSS scores of dual cigarette and cigar smokers were compared. The first group (n=13) smoked both cigarettes and little cigars (LC); the second group (n=22) smoked cigarettes and cigarillos (CG). Dual users answered the NDSS questionnaire twice - considering their cigarette and cigar smoking. Overall NDSS scores were correlated with the FTND score to determine the strength of the global relation. Profile analyses were used to determinedifferences in the component constructs as a function of the tobacco article used.
Results: There were significant correlations between FTND and the NDSS OS among FM, r=.54; PMM, r=.72; RYO, r=.51; all p<.05. Scores on S were significantly higher (p<.05) than scores for D, C, P and T all but there were no differences between the groups on the overall or any of the subscales scores. Analyses of the dual users indicated a significant correlation (p<.05) between overall NDSS and FTND for both CG (r=.46) and LC (r=.56) The NDSS subscale sores did not differ between the LC and CG and the profile analyses revealed no significant differences from parallelism.
Conclusions: These data suggest that although there are demonstrably different components of nicotine dependence these constructs do not differentiate between exclusive smokers of FM, RYO or PMM or cigar smokers.
Financial Support: Supported by grants from National Cancer Institute 1RO1CA138973 and 1RO1CA158045.

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SUBSTANCE USE DURING PREGNANCY AMONG YOUNG WOMEN WITH SYMPTOMS OF PSYCHOLOGICAL STRESS AND DEPRESSION.

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Aims: Risks associated with substance use during pregnancy include low birth weight, preterm birth, poor cognitive development, and behavioral problems. Young women, particularly young women with unplanned pregnancies, may be particularly vulnerable to ATOD use during pregnancy. Prior results suggest that women with unintended pregnancies smoke more than their peers whose pregnancies were planned. We evaluate the consequences of both unintended pregnancy status and stress/depression for ATOD use during pregnancy.
Methods: The Relationship Dynamics and Social Life (RDSL) study is based on a sample of 214 pregnant women, drawn from a larger population-based, random sample of 1,003 women in a Michigan county. The dataset includes weekly survey-based measures of stress and depression symptoms, as well as weekly measures of ATOD use, collected throughout their entire pregnancies.
Results: Our multivariate results suggest that women who experience stress or depression symptoms during pregnancy drink alcohol and smoke marijuana more during their pregnancy. Even when controlling for stress and depression levels prior to pregnancy, women were more likely to drink alcohol and smoke marijuana during stressful weeks. Interestingly, stress and depression were not related to smoking cigarettes during pregnancy. In addition, women with unintended pregnancies drank more alcohol and smoked more cigarettes during their pregnancy. Whether the pregnancy was intended or unintended, however, does not explain why stress and depression increase substance use during pregnancy. Whether the pregnancy was intended or unintended, however, affects alcohol consumption and cigarette smoking net of the stress and/or depression it may cause.
Conclusions: We find that young women with psychological symptoms and/or unintended pregnancies have higher levels of ATOD use during pregnancy. This study has implications for identifying young women at risk of ATOD use as well as pregnancy complications and negative birth outcomes.
Financial Support: Supported by NICHD R01 HD050329, NICHD R01 HD050329-S1, NIDA R21 DA024186, and NIDA contract HHSN271200900786P

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COCAINE IMAGES IMPACT INHIBITORY CONTROL: A WITHIN- AND BETWEEN-SUBJECTS COMPARISON.

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Aims: Inhibitory control is impaired in cocaine users after viewing cocaine images compared to neutral images. A limitation to examining the effect of image type on inhibition is the requirement to use a between-subjects design. This study sought to develop within-subjects methods to assess the impact of cocaine images on inhibitory control. We predicted subjects would show significantly impaired inhibitory control following cocaine images, but not following neutral images or a non-image cue (i.e., a rectangle as presented in the cued go/no-go task).
Methods: One group of subjects (n=13) completed the Attentional Bias-Behavioral Activation (ABBA) task wherein cocaine images were the go cue. A second group (n=13) completed the ABBA task during which neutral images were the go cue. Both groups completed a traditional cued go/no task with vertical rectangles as the go cue.
Results: Subjects in the cocaine go condition had a higher rate of inhibitory failures on the ABBA task compared to when they performed the traditional cued go/no-go task. Performance did not differ when subjects performed the ABBA task with neutral images and the traditional cued go/no-go task. Subjects who completed the ABBA task with cocaine images performed more poorly than their counterparts who completed this task with neutral images. The two groups did not differ significantly when they performed the traditional cued go/no-go task.
Conclusions: These results replicate previous findings showing impaired inhibitory control after viewing a cocaine image. Moreover, the consistent rate of inhibitory failures between the neutral image condition of the ABBA task and traditional cued go/no-go task suggests that the cued go/no-go task can be substituted for the neutral go condition of the ABBA task, allowing a within-subjects design to be used to more efficiently evaluate the influence of other manipulations on inhibitory control. We plan to enroll a total of 50 subjects.
Financial Support: NIDA R01 DA025032 (PI: CRR)

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ENERGY DRINK CONSUMPTION AND OTHER DRUG USE IN MALE AND FEMALE EIGHTH, TENTH, AND TWELFTH GRADERS.

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Aims: Energy drink (ED) use in college students has been linked to heavy/problem drinking and other drug use (e.g., Arria et al., 2011). The present study examined the relationship between ED consumption and other substance use in a younger cohort of male and female eighth, tenth, and twelfth grade students.
Methods: Participants were eighth (N=1248), tenth (N=810), and twelfth (N=839) graders attending Chesterfield County, Virginia public schools. Students completed a survey using a computer scored answer sheet. Domains included demographics, personal attitudes, substance use, peer influences and family functioning. The present study focused on the N=128 survey items targeting substance use (i.e., caffeine, tobacco, alcohol, drugs).
Results: Overall, 70.77% of students used EDs at least once and 12.54% were regular ED users (6+ days in past month). Males were more likely to be regular ED users than females (13.99% and 11.08%, respectively; p=.02). The percentage of adolescents who consumed EDs at least once increased from 64.50% in eighth grade to 73.50% in tenth grade, and 77.45% in twelfth grade. Across grades, regular ED users were more likely than the other students to have used: alcohol (63.04% vs. 40.37%); marijuana (48.35% vs. 25.06%); LSD (14.29% vs. 3.81%); cocaine (9.34% vs. 1.79%); inhalants (23.63% vs. 9.80%); methamphetamines (5.51% vs. .78%); amphetamines (20.05% vs. 8.39%); sedatives (21.70% vs. 6.03%); tranquilizers (13.46% vs. 3.62%); prescription narcotics (17.26% vs. 6.34%); heroin (4.95% vs. 0.62%); and ecstasy (8.49% vs. 3.03%) (all p<.001). They were also more likely to smoke cigarettes (52.05% vs. 24.32%). These relationships were found in both male and female students.
Conclusions: Regular ED use was associated with use of nearly all other substances including tobacco, alcohol and other drugs. This was true for both male and female students. Results suggest ED use may help to identify adolescents at risk for other substance use.
Financial Support: Drug Free Communities Support Grant from the Office of National Drug Control Policy.

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METHAMPHETAMINE DEPENDENCE AND INTENSIVE MOTIVATIONAL INTERVIEWING.

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Aims: Motivational interviewing (MI) has been shown to be effective as a short-term therapeutic intervention for alcohol abuse. However, the research on the effectiveness of MI for other drug populations is mixed. The inconsistent findings may, in part, be due to the severity of problems experienced by these populations and the relative brevity of the 1-3 sessions typical of an MI intervention. The current study is a Stage 2 clinical trial that addresses these gaps in the literature by studying a methamphetamine (MA) dependent population and extending MI therapy to 9 sessions.
Methods: Participants were randomized to 1) a 9-session intensive MI intervention (n=111) or 2) one session of standard MI with a time equivalence activity (n=106). All participants were followed at 2, 4, and 6 months. Data collection included days of MA use, ASI drug, and ASI psychiatric severity.
Results: Longitudinal analyses were estimated via the use of random intercept models assessing averaged treatment effects from baseline. Both conditions had significant decreases in MA use and ASI drug scores though significant differences between MI conditions were not observed. However, ASI psychiatric severity scores significantly declined for the intensive MI condition but not for the standard MI condition. Further examination of psychiatric symptoms showed significant decreases in the number of days of psychological problems compared to the standard MI condition and significant decreases in the number of days of depression for the intensive MI condition.
Conclusions: This clinical trial focused on MA dependent individuals, a population that frequently presents with serious psychiatric symptomatology at treatment entry, thereby complicating treatment efforts. Our findings demonstrate that standard MI may be equally beneficial in helping MA clients reduce their MA use and problem severity but intensive MI may help alleviate psychological problems not adequately addressed in shorter MI interventions. Future study should include long-term follow-up and examine the elements of MI therapy that may work as moderators to successful recovery.
Financial Support: NIDA R01 DA024714

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PRESCRIPTION DRUG USE, IMPAIRMENT WARNINGS, AND PERCEIVED RISKS AMONG U.S. DRIVERS.

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Aims: Estimate the use of potentially impairing prescription drugs among U.S. drivers, determine exposure to impairment warnings, and characterize perceived risk of related adverse driving events.
Methods: The study was nested within the 2013 National Roadside Survey (NRS). The NRS uses stratified random sampling to select 60 sites across the continental U.S. for data collection. Drivers at these sites are randomly stopped and asked to complete a survey regarding their driving, alcohol use, and drug use.
Results: Overall, 6,279 drivers consented to NRS participation in 44 sites; of these, 5,301 (84%) completed the prescription drug questionnaire. The most commonly reported prescription drugs used during the past 24 hours were antidepressants (8%), pain killers (3%), sleep aids (3%), benzodiazepines (2%), morphine (2%), ADHD medications (2%), and muscle relaxants (1%). A majority of the drivers who used these drugs also reported receiving a warning from a health care provider or package label regarding the potential for impaired driving. Such warnings were most common for muscle relaxants (91%), sleep aids (87%), and pain killers (82%). Despite these warnings, the perceived risks of driving while using these medications was relatively low. For example, among drivers that reported using pain killers only a slight majority thought it likely or very likely that, when taken as prescribed, these drugs could affect safe driving (63%), cause a crash (58%), or lead to arrest (56%) and conviction (56%) for impaired driving.
Conclusions: Not all drivers who report recent use of potentially impairing prescription drugs recall receiving warnings about the risks of driving while using these drugs. Furthermore, many drivers who do receive these warnings do not perceive it likely that these drugs, when taken as prescribed, could affect their driving or lead to a crash, arrest, or conviction for impaired driving. This suggests the need for interventions that better relay the risks involved in driving while using prescription drugs with impairment potential.
Financial Support: National Highway Traffic Safety Administration and the National Institute on Drug Abuse

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CAFFEINE WITHDRAWAL IN COLLEGE STUDENTS: DIFFERENCES BY GENDER AND BEVERAGE TYPE.

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Aims: The purpose of this study was to examine whether reports of caffeine withdrawal varied by gender and type(s) of caffeinated beverages consumed in a sample of college freshmen. We hypothesized that women, and those consuming coffee and/or energy drinks (e drinks) would be most likely to report symptoms of caffeine withdrawal.
Methods: Participants were N=1589 freshmen (age 18 and older) who completed an on-line research survey (Spit for Science*) and reported recent caffeine use. The present study focused on survey demographic items, type(s) of caffeinated beverages consumed (coffee, tea, sodas, energy drinks (e-drinks) and occurrence of caffeine withdrawal symptoms (e.g., headache, fatigue, anxiety, depression, and/or nausea after stopping all caffeine for a day or more). Descriptive statistics were used to characterize caffeine use and occurrence of caffeine withdrawal. Chi-square analysis was used to examine gender differences in withdrawal across different caffeine beverage types.
Results: One-fifth (20.6%) of current caffeine users reported 1+ symptoms of withdrawal, with headaches most prevalent (15.6%), followed by fatigue (13.0%); anxiety (3.7%); depression (1.6%) and nausea/vomiting (1.1%). Females were more likely than males to report withdrawal (22.9% vs 16.2%; p<.002), and more women reported headaches (17.6% vs 11.7%) and fatigue (14.9% vs 9.5%) than men (both p<.002).
Coffee and e-drink users were most likely to report withdrawal. Among coffee drinkers, women continued to report caffeine withdrawal at higher rates than men (27.6% vs 21.5%; p<.04). Similarly, among e-drink consumers, women were twice as likely as men to report caffeine withdrawal (37.0% vs 18.6%; p<.002). This pattern was found not only for the individual symptoms of headaches and withdrawal, but also for depression, with more women (7.5%) than men (0.7%) reporting this symptom (p<.003).
Conclusions: As predicted, female caffeine users were more likely to report symptoms of caffeine withdrawal than male users. These gender differences were most pronounced, however, among those who consumed e-drinks.
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IMMEDIATE IMPACT OF HURRICANE SANDY ON PEOPLE WHO INJECT DRUGS IN NEW YORK CITY.

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Aims: Natural disasters and other "big events" can affect drug use, and the epidemiology of HIV and other blood-borne infections. Hurricane Sandy had a broad immediate impact on New Yorkers, and may have increased drug-related HIV transmission risks. We examined how the storm affected drug use and HIV transmission risks among people who inject drugs (PWID).
Methods: As part of an ongoing study, we interviewed 300 PWID in New York City about their drug use, living circumstances, actions they took, and actions of others during Hurricane Sandy and in the subsequent week.
Results: In the week following the storm 60% of participants were unable to obtain drugs to avoid withdrawal on one or more days; 25% shared syringes or drug preparation equipment and 15% injected drugs with people that they normally would not inject with due to problems related to the storm. Of HIV-positive PWID, 43% missed HIV medication doses. Of PWID on methadone or buprenorphine maintenance therapy, 55% were unable to obtain sufficient take-home doses and experienced withdrawal. Among those with domiciles, 26% lost electrical power, 25% lost heat and 4% lost running water. One fifth of participants rescued others from floods, accidents or other serious threats, 59% helped others obtain food or other necessities and 21% volunteered with aid groups.
Conclusions: Hurricane Sandy appears to have interfered with HIV treatment and drug treatment, and increased risks of transmission of HIV and other blood-borne infections for PWID. Despite hardships, PWID served as assets to their respective communities, helping other drug users and non-drug users in the wake of the storm. Big events, including hurricanes and other natural disasters, can alter physical and social environments, affect risk behaviors and contexts, and perhaps contribute to shaping HIV epidemic dynamics. Research on long-term effects is needed.
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PREDICTING MOOD AND CRAVING FROM REAL-TIME NEIGHBORHOOD SURROUNDINGS.

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Aims: Mobile, real-time interventions could be based on live predictions of changes in mood and craving. In a Geographical Momentary Assessment (GMA) study with real-time self-report (Ecological Momentary Assessment, EMA) and location (GPS) data, we found that the strength of the relationships between neighborhood characteristics and participants' mood and craving increased with inclusion of GPS track data from up to about 5 hrs prior to each self-report. Here we tested whether GPS track data could predict the contents of self-reports into the future, as a live intervention would need to do.
Methods: We collected GPS data and EMA ratings of mood, stress, and drug craving for 16 weeks in 27 methadone-maintained polydrug users. Participants' tracks were calculated for the 12 hrs before each EMA entry. We used a random-Forest machine-learning model to predict EMA responses (stress, heroin craving, and negative and positive mood) 30, 60, and 90 min into the future. Each model used 5 hrs of track data, omitting the 30, 60, or 90 min of data immediately preceding the entry. We varied the proportions of the data used for the training and validating the models.
Results: We matched 3,711 randomly prompted EMA entries to locations. Future-predicting model accuracy was very high for prediction of positive and negative mood scores (R values typically 0.70 to 0.97), moderate for prediction of stress (kappas typically 0.50 to 0.65), and low for prediction of heroin craving (kappas typically 0.20 to 0.35).
Conclusions: These results provide initial support for use of GPS tracks as part of an algorithm to predict, intervene, and perhaps prevent, changes in mood and stress. Further work is needed to replicate this finding and to improve prediction of craving.
Financial Support: This work was supported by the Intramural Research Program of NIDA, NIH.

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PREFRONTAL AND PARIETAL VOLUMES AND COGNITION IN EMERGING ADULT MARIJUANA USERS.

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Aims: Initiation of marijuana (MJ) use coincides with brain neuromaturation. Chronic use among adolescents has been associated with structural and functional abnormalities, particularly in regions responsible for higher order cognition and densely populated with cannabinoid receptors. Here, we investigated prefrontal (PFC) and parietal volumes and cognition in emerging adult MJ users and explored potential gender differences.
Methods: Participants were 27 MJ users and 32 controls ages 18-25 without neurologic or psychiatric disorders, heavy other drug use, or left-handedness. PFC and parietal volumes were obtained from high-resolution images processed in FreeSurfer. Cognitive variables included complex attention and cognitive inhibition. Series of multiple regressions examined whether group status, past year MJ, and their interactions with gender predicted ROI volumes. Post-hoc analyses were brain-behavior correlations between ROIs and cognitive variables and Fisher's z tests to assess group differences.
Results: After controlling for intracranial volume, BMI, verbal IQ, gender, alcohol, hallucinogen and nicotine use, MJ users exhibited significantly smaller medial orbitofrontal (mOFC; p=.004) and inferior parietal volumes (p=.04); increased past year MJ *dose-dependently* predicted smaller mOFC volume (p=.05). There were no significant gender interactions. Smaller mOFC volumes were associated with poorer complex attention in MJ users (p<.05).
Conclusions: Regional findings suggest disruption of typical neurodevelopment processes associated with regular MJ use for both genders. Group differences in the inferior parietal region warrant further exploration of premorbid factors among teens that initiate use. These results highlight the need for longitudinal, multi-modal imaging studies providing clearer information on timing of neurodevelopmental processes and neurocognitive impacts of youth MJ initiation.
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PREDICTORS OF ILLICIT DRUG USE IN LOW-INCOME AFRICAN-AMERICAN WOMEN: A MULTILEVEL ANALYSIS OF DEMOGRAPHIC AND CULTURAL FACTORS.

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Aims: Low-income African American women live at the intersection of multiple marginalized statuses, and may be disproportionately exposed to negative stressors associated with their gender, race, and class. However, insufficient research has examined how these stressors, like victimization, financial crises, and gendered racism (experiences of sexism compounding racism), influence illicit drug use among this population. Using longitudinal data, this study investigates the effects of characteristics and experiences especially relevant for low-income African American women on their illicit substance use.
Methods: Data for this study were collected at four time points (intake, 6, 12, and 18 month follow-up) from a community, probation, and prison-based sample of African American women (N=514). Multilevel mixed-effects regression with Stata's xtmixed command is used to predict illicit drug use (logged composite score) on select independent variables. Other relevant sociodemographic and control variables are also included.
Results: Results of the full model indicate that alcohol use in the past 6 months and having a history of drug problems result in greater drug use (1.44, p>0.001 and 1.37, p>0.001), while being older and more educated are inversely related to drug use (-0.03, P>0.001 and -0.07, p>0.05). Importantly, gendered racism is significant in the full model, such that more experiences of gendered racism result in greater drug use (0.02, p>0.05). Experiencing a financial crisis and parental history of drug problems are predictive of drug use in restricted models, but not the full model.
Conclusions: Findings suggest that while traditional predictors of illicit drug use like age and education may hold for African American women, adverse experiences associated with living at the intersection of multiple disadvantaged statuses may also trigger drug use. Intervention efforts should incorporate this knowledge into approaches to combat addiction among low-income African American women.
Financial Support: Research funded by the National Institute on Drug Abuse (R01-DA022967, PI: Oser).

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DELAY DISCOUNTING IN CURRENT, EX, AND NON-SMOKERS: INTERACTIONS WITH GENDER.

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Aims: Many factors, such as age, socioeconomic status, and substance use, have a known association with delay discounting measures. Smokers have been shown to discount the future more than non-smokers and equivocal results have been revealed in examinations of gender and discounting rates. The aim of the current study was to elucidate differences in delay discounting rates among a large sample of individuals who have never smoked cigarettes, quit smoking for any amount of time, and currently smoke. We hypothesized that there would be no difference in discounting between men and women and that individuals who have never smoked would discount less than ex and current smokers.
Methods: A sample of 1305 Amazon Mechanical Turk users completed an online survey including multiple questionnaires and a delay discounting task evaluating choices among immediate smaller monetary amounts and larger delayed amounts.
Results: A 3 (smoking status) X 2 (gender) between subjects ANOVA revealed a significant main effect of smoking status and a significant interaction between smoking status and gender. Current smokers discounted more than ex and non-smokers, while ex-smokers discounted more than non-smokers. The interaction between gender and smoking status revealed female ex-smokers discounted less than male ex-smokers. Interestingly, female smokers discounted more than male smokers. No gender differences were revealed in the group of non-smokers.
Conclusions: These preliminary results suggest differences in decision-making skills between individuals with different smoking statuses in addition to a possible gender difference in discounting rates among smokers and ex-smokers.
Financial Support: NIDA (R01DA034755) and Virginia Tech Carilion Research Institute

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EFFECTS OF OMEGA-3 FATTY ACIDS ON TOBACCO CRAVING: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PILOT STUDY.

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Aims: Cigarette smoke induces an oxidative stress with subsequent polyunsaturated fatty acids (PUFA) peroxidation. Low concentration of Omega-3 PUFA can affect neurotransmission, resulting in hypofunctioning of mesocortical systems associated in reward and dependence mechanisms. Omega-3 PUFA deficiency, in particular eicosapentaenoic acid (20:5 n-3, EPA) and docosahexaenoic acid (22:6 n-3, DHA) was linked to reduced psychological health and stress coping. Although stress is well linked to smoking urges and behavior, no research to date examined PUFAs supplementation effects on tobacco craving. The purpose of this study was to assess effects of DHA and EPA as an add-on novel supplement on tobacco craving in regular cigarette smokers.
Methods: We studied the effect of a daily administration of oral treatment with 2710mg EPA/day and 2040 mg DHA/day for 1 month on subjective craving in 48 healthy regular smokers on three occasions (day0:baseline, day30 and day60). The study was carried out according to a randomized, placebo-controlled, double-blind design.
Results: PUFA significantly lowered tobacco craving after 1 month of treatment when compared to baseline. Craving did not return to baseline values in the month that followed treatment discontinuation.
Conclusions: This is the first study demonstrating that Omega-3 PUFA supplementation reduce tobacco craving in regular smokers compared to placebo treatment. As most available pharmacological treatments to smoking harm reduction and cessation are associated with side effects and low efficacy, the development of new strategies and treatments is necessary. This finding suggests that Omega-3 PUFA may be of benefit in helping smokers reduce tobacco consumption before quitting. Further studies are needed on larger samples to explore possible therapeutic implications on heavy cigarette smokers.
Financial Support: This study was not funded by any outside source

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ABSENCE OF STRESS DYSREGULATION PREDICTS COCAINE AND MOOD OUTCOMES IN A STUDY OF MIRTAZAPINE FOR DEPRESSED COCAINE-DEPENDENT PATIENTS.

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Aims: Does stress dysregulation - assessed by diurnal cortisol secretion profile - affect early abstinence, cocaine, and mood outcomes for depressed cocaine-dependent patients?
Methods: The data arises from an 8-week, double blind, placebo-controlled trial of mirtazapine (MIR, 60 mg/day) for depressed cocaine-dependent patients. Before randomization, participants had a 2-week lead-in when they could earn vouchers contingent on abstinence. On day 1, saliva cortisol samples were collected at 9am, 1 pm, 4pm. "Typical" diurnal cortisol profiles exhibit a high AM peak followed by a pm decrease. Deviations from this profile were "Atypical", suggesting dysregulation. With the lead-in completed, subjects were randomized (42 MIR/44 PBO) and stratified according to abstinence and mood status. Cocaine outcomes were a) 75% reduction in use versus baseline; b) three weeks of continuous abstinence. Mood outcome was 50% reduction in Ham-D score from baseline.
Results: 1: At the end of the lead-in, 21/32 abstinent and 16/41 not-abstinent patients displayed a Typical diurnal cortisol profile. ($\chi 2 = 5.09$, $p < 0.02$).
2: Abstinence at the end of the lead-in predicted abstinence (OR = 30.3), reduction in cocaine use (OR = 3.9), and mood improvement (OR = 3.17) in the 8-week trial, controlling for medication.
3: Mirtazapine was not superior to placebo for mood (Wald $\chi 2 = .027$, $p > 0.868$) or cocaine (Wald $\chi 2 = 1.13$, $p > 0.288$) outcomes.
Conclusions: 1: Absence of stress dysregulation (Typical cortisol profiles) predicted early abstinence.
2: Early abstinence dictated all cocaine and mood outcomes, regardless of medication assignment.
3: Stress dysregulation may discriminate early from late-responders or non-responders among cocaine dependent patients.
Financial Support: This research is supported by K23DA277044 to Dr. Raby, and P50-DA09236 to Dr. Kleber

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INFLUENCE OF PHARMACOKINETICS ON THE ABUSE LIABILITY OF CONTROLLED-RELEASE OPIOID FORMULATIONS: THE CASE OF OXYCODONE.

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Aims: Oxycodone is an opioid with a known abuse liability that produces prototypical opioid effects. Pharmacokinetic parameters such as peak drug plasma concentration (Cmax) and the time to reach Cmax (Tmax) are associated with the onset and magnitude of positive subjective drug effects. The absorption profiles of opioid formulations influence these pharmacokinetic parameters, particularly with immediate-release compared to controlled-release products, however, this may also be the case within different controlled-release formulations. To date, there has only been one abuse liability study of oxycodone that evaluates both its pharmacokinetics (PK) and positive subjective effects (pharmacodynamics, PD). A review of the literature was conducted to better understand the abuse liability of oxycodone formulations by examining the relationship between PK parameters and the positive subjective effects reported in 19 studies (i.e., 2 PK/PD, 10 PD, and 7 PK studies). The studies examined evaluated different formulations of oxycodone (immediate-release, controlled-release, and tamper-resistant controlled release formulations), dosages, and routes of administration (oral, intravenous and intranasal).
Conclusions: Current evidence suggests that both dose and formulation of oxycodone can influence positive subjective effects. Very few published studies have evaluated the abuse liability of controlled-release oxycodone formulations taken intact orally, however existing studies suggest positive subjective effects are identified. In addition, differences in the absorption-related PK parameters of oxycodone formulations suggest there may be variation in abuse liability. It is recommended that future studies provide both pharmacokinetic and positive subjective effects data in assessing the abuse liability of oxycodone formulations.
Financial Support: None

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HIGH DEAD-SPACE SYRINGE USE AMONG PEOPLE WHO INJECT DRUGS IN TIJUANA, MEXICO.

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Aims: High dead-space syringes (HDSS) are believed to confer an elevated risk of acquiring HIV and other blood-borne infections. We identified prevalence and correlates of high dead-space syringe use among people who inject drugs (PWID) in Tijuana.
Methods: Beginning in 2011, PWID who reported being 18 years or older who injected drugs within the last month were recruited. At baseline and semi-annually, PWID underwent HIV testing and interviewer-administered surveys. Logistic regression was used to identify correlates of using HDSS.
Results: Of 557 PWID, 40% had used HDSS. Most (72%) had done so because no other syringe type was available or because they were easier to get (20%). Controlling for sex and age at first injection (AOR:0.97 per year; 95%CI:0.94-1.00), use of HDSS was associated with cocaine as first drug injected (AOR:2.68; 95%CI:1.15-6.22), having been stopped or arrested by police (AOR:1.84; 95% CI:1.11-3.07), being deported from the US (AOR=1.64; 95%CI:1.06-2.53), and believing it is illegal to carry syringes (AOR=1.78; 95%CI:1.01-3.15).
Conclusions: Use of HDSS by PWID is surprisingly common in Tijuana, which could increase transmission of HIV and viral hepatitis. Efforts are needed to expand coverage of low-dead space syringes at syringe exchange programs and pharmacies. Education is required to increase awareness of the harms associated with HDSS, and to reassure PWID that syringe possession is legal across Mexico.
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PREVALENCE OF MILD TRAUMATIC BRAIN INJURY IN COCAINE-DEPENDENT RESEARCH VOLUNTEERS.

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Aims: There is a high prevalence of mild traumatic brain injury (mTBI) among those with substance dependence. Increased impulsivity and disinhibition are common consequences of both substance abuse and brain injury. Patients with mTBI may be predisposed to substance abuse and vice-versa. Thus, in this study we determined the prevalence of self-reported mTBI in a group of cocaine-dependent subjects (n=95) as well as healthy volunteers (n=75) recruited from a similar demographic setting. Additionally, we examined the relationship between mTBI and clinically relevant correlates, including impulsivity, cocaine use history, and treatment outcome in the cocaine-dependent group
Methods: Information about the participants' demographic and drug use history was collected at the intake interview. Presence of mTBI was assessed on a Closed Head Injury (CHI) scale and impulsivity was measured using the Barratt Impulsiveness Scale (BIS-11). Finally, treatment outcome amongst cocaine-dependent treatment seekers was computed as the treatment effectiveness score (TES).
Results: A higher proportion of cocaine-dependent individuals (29.5%) reported mTBI in their lifetime compared to controls (8%). Among cocaine users, the average age of sustaining mTBI was significantly lower that the age of onset of cocaine use. Presence of mTBI was not associated with higher impulsivity or self-reported years of cocaine use. No differences were noted on treatment outcome as measured by the TES between cocaine users with mTBI and their non-TBI counterparts, but small sample sizes limited proper statistical comparisons on treatment outcome.
Conclusions: These results extend previous findings that have shown a high prevalence of mTBI among individuals with substance use disorders to individuals with a primary diagnosis of cocaine dependence and highlights the importance of screening for head trauma as a complicating factor in the treatment of substance use disorders.
Financial Support: NIDA Grant DA009262 (PI Moeller)

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GENE VARIANTS OF THE OPIOID SYSTEM - RELATIONSHIP TO HEROIN SELF-EXPOSURE, ADDICTION, AND TREATMENT.

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Aims: To determine whether specific variants in genes of the opioid system are associated with heroin addiction in a unique cohort that includes subjects who self-exposed without becoming addicted and chronic treatment-resistant heroin-dependent subjects, offered heroin-assisted treatment.
Methods: The subjects consisted of four groups: 1) subjects with no history of drug use (n=197); 2) subjects self-exposed to illicit opiates at least 5 times but not addicted (n=198); 3) former heroin-dependent subjects successfully methadone-maintained (n=204); and 4) treatment-resistant heroin-dependent subjects, offered heroin-assisted treatment (n=196). Genotyping of 82 single nucleotide polymorphisms (SNPs) from 8 genes was performed using a custom made GoldenGate array (Illumina, San Diego, CA) or pre-designed TaqMan SNP genotyping assays (Applied Biosystems, Foster City, CA). A one-way ANOVA was performed to test for differences in genotype frequency between the four groups for each SNP separately. SNPs that showed a significant ($p<0.05$) difference in the ANOVA were further analyzed with contingency tables, calculating chi-square for each 'case' group versus controls.
Results: One SNP, rs548339 in *OPRM1*, was found to have a point-wise significant difference in genotype frequency between the four groups ($p<0.05$). Comparing each of the "case" groups separately to the controls for rs548339, the methadone-maintained subjects had a significantly ($p=0.0288$) greater number of individuals with genotype CC.
Conclusions: *OPRM1* intronic SNP, rs548339, previously associated with both depressive symptoms and alcohol dependence, may be associated with heroin addiction.
Financial Support: Pilot funds from NIDA [MJK], CCBH and ZonMw 310000465 (PB, JVR, & WVDB)and from The Adelson Medical Research Foundation (MJK)

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POSTERIOR PREDICTIVE POWER: A DECISION-MAKING TOOL FOR CLINICAL TRIAL DESIGN.

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Aims: Conventional clinical trial design is guided by power calculations that are conditional on a given treatment effect size, but these calculations fail to account for the uncertainty in the effect size. Posterior predictive power explicitly accounts for this uncertainty by integrating over the range of possible effect sizes given the available evidence. This methodological paper demonstrates the ease of posterior predictive power analysis using data readily available from the literature. We present simulation study results to assess the relative merits of posterior predictive power over conventional power analysis.
Methods: The published results from a randomized clinical trial of vigabatrin for the treatment of cocaine dependence provide the prior evidence. This analysis takes the perspective of investigators designing a follow-up study. Conventional power analysis conditional on the point estimate from the reported trial is compared to posterior predictive power analysis.
Results: Standard power analysis leads to the conclusion that n=82 is sufficient to yield >80% power to reject the null hypothesis at the $p = 0.05$ level. However, Monte Carlo simulations reveal that once effect size uncertainty is incorporated into the analysis, n = 190 is required to yield >80% power. Failure to account for the range of possible effect sizes can lead to overestimation of the chances of success in a trial.
Conclusions: Posterior predictive power provides a formal method to quantitatively account for effect size uncertainty in clinical trial design, making it a valuable decision-making tool for allocating scarce resources.
Financial Support: NIDA Grant P50 DA009262

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CRF VERSUS AVP IN HUMAN STRESS RESPONSIVITY: INITIAL STUDIES.

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Aims: Arginine vasopressin (AVP) (along with oxytocin), was discovered and shown to have a major role in renal function and also to activate the hypothalamic-pituitary-adrenal (HPA) axis in the early 1950's (du Vigneaud). Corticotrophin releasing factor (CRF), elucidated much later, became the most commonly used HPA activator in neuroendocrinology studies. Recently studies have been conducted in animal models on the possible role of AVP in addictive diseases, but no studies to date have been on its possible role in human addictive diseases. AVP is not approved by the FDA for intravenous (IV) use. The aim of this study was to conduct initial pilot studies on dose-ranging of AVP (intramuscular, IM), with two doses vs two IV doses of CRF in healthy volunteers (n=15), as well as in drug-free former cocaine-dependent persons (DFFCD)(n=4).
Methods: AVP doses were 0.36 and 0.60 mcg/kg (IM), and for CRF 0.5 and 2.0 mcg/kg (IV). We calculated the area under the curve (AUC) for stimulation of ACTH and cortisol from 0-120 minutes after injection.
Results: For ACTH, there was a main effect of dose (0, low, high; $p<0.00005$), but no significant difference between AVP and CRF (2-way ANOVA, challenge type x dose, repeated measures of dose). Post-hoc tests revealed significant differences between CRF placebo, low, and high doses ($p<0.05$), but no differences between AVP low and high doses. For cortisol, there was a main effect of dose on cortisol AUC ($p<0.00001$). Post-hoc tests revealed no difference between low AVP and CRF doses, or between high AVP and CRF doses. There was no difference between low and high AVP doses, whereas there was a significant difference between low and high CRF doses ($p<0.005$). There were no differences noted between AVP and CRF in the DFFCD subjects.
Conclusions: There was no substantial difference between the extent of ACTH and cortisol stimulation by AVP versus CRF in healthy volunteers. Further studies with additional subjects are necessary for definitive evaluation of whether this relationship holds in the DFFCD cohort.
Financial Support: Adelson Medical Research Foundation, NIH-NCATS grant UL1-TR000043 (CTSA).

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MODELING CAUSAL RELATIONSHIP BETWEEN MEMORY AND CRAVING-RELATED BRAIN NETWORKS IN NON-TREATMENT SEEKING COCAINE SMOKERS USING IMAGES, A GRAPH THEORETIC APPROACH.

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Aims: Although functional magnetic resonance imaging (fMRI) research is widespread, studies on effective connectivity or the causal relationship between brain areas is little studied. Currently, only two studies in the cocaine fMRI literature have examined causal relationship among brain regions [Zhang et al., 2006 (reward circuits); Ma et al., 2012 (working memory)]. Zhang used a Bayesian search method that could fit only five brain regions due to computational constraints. In this study, we used a graph theoretic approach called IMaGES (Ramsey et al., 2011) that utilized a computationally powerful Bayesian search algorithm that was able to compute connectivity of seven brain regions in modeling the causal relation between memory- and drug craving-related brain networks that likely contribute to drug use in non-treatment seeking cocaine smokers.
Methods: The brains of 20 cocaine smokers (29-53 yrs; 15M; 5F; abstinent from cocaine for 72 hrs) and 17 age-, education-, and ethnically-matched healthy control participants (25-53 yrs; 13M; 4F) were scanned using a Siemens 3T magnet during the performance of a visual cue exposure task that included cocaine and neutral cues. The experimental design allowed for the assessment of both memory and craving processes. For the graph analysis, time series data were extracted from significantly activated brain regions, as determined through GLM analysis, and used as input to IMaGES.
Results: During exposure to cocaine cues, cocaine smokers but not controls showed a feed-forward connectivity from the memory- to the craving-related brain networks.
Conclusions: Effective connectivity analysis of brain regions involved in memory and craving provides insight into the mechanism underlying substance use disorder that can lead to the development of treatment targets and individually tailored interventions.
Financial Support: Research was supported by NIDA K01DA029047.

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INFLUENCES OF BEHAVIOR AND ACADEMIC PROBLEMS AT SCHOOL ENTRY ON MARIJUANA USE DURING ADOLESCENCE AMONG AFRICAN AMERICANS.

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Aims: African-American children are at increased risk for school behavior problems and lower academic achievement. The aim of this study was to examine how the co-occurrence of these problems at school entry might impact marijuana use during adolescence.
Methods: Primarily low-income, urban dwelling African-American children entering first grade were interviewed as part of a longitudinal field study (n=458). Latent class and latent transition analyses were conducted to examine patterns of academic and behavior problems in first grade and their influence on transitions in marijuana involvement between 6th and 9th grades.
Results: Two problem classes emerged at school entry; a class of youth with primarily externalizing behavior problems (27%) and a class with attention, concentration and academic difficulties (12%). Youth with attention, concentration and academic difficulties were more likely to rapidly transition from no marijuana involvement to use and problems between 7th and 8th (AOR=10.7, 95% CI=1.7, 66.1) and 8th and 9th grades (AOR=3.5, 95% CI=1.0, 12.8) and more likely to transition to use and problems given the opportunity to use marijuana early in high school compared to youth with no problems (AOR=6.0, 95% CI=1.4, 26.1). Youth with externalizing behavior problems at school entry were significantly more likely to transition from no use to having a marijuana opportunity during the transition to high school compared to youth with attention, concentration and academic problems (AOR=7.2, 95% CI=1.2, 41.9).
Conclusions: These findings highlight the importance of developing targeted prevention programs that address aspects of school readiness associated with the characteristics of the identified problem classes and the need to expand early interventions to include low-income, minority youth who may be entering school less ready than their non-minority peers.
Financial Support: R01 DA032550

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CLINICIAN BELIEFS AND BEHAVIORS REGARDING SCREENING AND BRIEF INTERVENTION FOR DRUG USE OF THEIR COMMUNITY HEALTH CENTER PATIENTS.

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Aims: Integration of behavioral health including substance use problems into primary care is an essential benefit that federally qualified health centers (FQHCs) will offer as part of the Affordable Care Act (ACA). This study explores FQHC primary care clinicians' beliefs and behaviors in integrating drug use assessment and treatment into their practices with a screening, brief intervention and referral to treatment (SBIRT) protocol.
Methods: We administered a 10-minute questionnaire to 68 primary care clinicians of 5 FQHCs in Los Angeles.
Results: Clinicians expressed limited confidence in their ability to deal with illicit drug use of their patients, scoring on average 3.31 on a five point Likert scale. Two-thirds reported assessing for drug use regularly 'at every visit' and/or 'at annual visits'. Median response for how often they counsel regarding drug use (on a five point Likert Scale from 'Never' to 'Always'), was 4 ('Usually'). Regarding their perspectives on the best practical resource for addressing drug use in their clinics, 45.6% named primary care clinicians. A minority (29.4%) of clinicians had completed a clinical rotation dealing with substance use, and 27.2% reported that more than 10 hours of their training was devoted to substance use problems. Having a substance use rotation was associated with greater confidence in SBIRT ($p<0.01$). More hours of substance use training was associated with greater confidence ($p=0.01$) and routinely addressing substance use in their patients ($p=0.04$).
Conclusions: Our findings suggest that clinician confidence and practices in substance use care are not optimal, but are associated with increased substance use education. Further work should examine whether improving clinicians' education/training at community health centers, improves substance use care practices.
Financial Support: This study is part of the UCLA Quit Using Drugs Intervention Trial (QUIT), which has been funded by National Institute on Drug Abuse (R01DA022445). Dr. Anjani Reddy is a National Research Service Award Fellow.

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EXAMINING VULNERABILITY TO SMOKELESS TOBACCO USE AMONG ADOLESCENTS AND ADULTS WITH MAJOR DEPRESSIVE DISORDER.

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Aims: Smoking prevalence is unevenly distributed in the U.S. population, with those with mental illness, other substance use disorders, and lower socioeconomic status being especially vulnerable. Less research has been conducted on the association between these same vulnerabilities and smokeless tobacco (ST) use. The present study examined ST use among adolescents and adults with major depressive disorder in the National Survey on Drug Use and Health (NSDUH).
Methods: Utilizing the most recent (2011) NSDUH, we compared odds for current cigarette smoking and ST use among adolescents and adults meeting criteria for past year major depressive disorder to the general population, after adjusting for potential confounding influences of sociodemographic and other substance use characteristics.
Results: Odds for current cigarette smoking among those classified with major depressive disorder were increased among adolescents (OR = 1.33 [0.97, 1.83], p = 0.021) and adults (OR with 99% CI = 1.70 [1.40, 2.07], p < .0005), while odds for current ST use did not differ among adolescents (OR = 0.90 [0.46, 1.76], p = 0.678) and were lower among adults (OR = 0.68 [0.46, 1.00], p = 0.01).
Conclusions: Major depressive disorder is associated with increased risk for smoking but not ST use among adolescents and adults demonstrating heterogeneity in predictors of vulnerability to use of different tobacco products.
Financial Support: This research was supported by National Institutes of Health (NIH) Institutional Training Grant T32DA07242, Centers of Biomedical Research Excellence Center Grant P20GM103644, and Fogarty International Center / NIH Grant K01TW008410. While the research reported in this publication was supported by NIH, FDA, and Fogarty International Center, the content is solely the responsibility of the authors and does not necessarily represent the official views of the funding agencies and institutes.

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IMPLICATIONS OF DECISION-MAKING PROCESSES FOR IMPROVING CONTINGENCY MANAGEMENT.

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Aims: Contingency Management is a successful drug addiction treatment that provides tangible alternative rewards contingent upon a decision to stay abstinent. The original basis for Contingency Management comes from the idea that drugs are economically-driven reinforcers. Subjects are given monetary rewards for submitting drug-free urine samples. Based on the pre-clinical and clinical data, we contend that these monetary rewards provided to Contingency Management subjects are too low in nominal value to cause the change of drug consumption observed in treatment.
Methods: We created a model using demand curves from cocaine users and show that the rewards provided in Contingency Management do not produce a significant enough change in cost to explain the effect that Contingency Management has on drug consumption.
Results: The monetary rewards used are inadequate to explain the observed success of Contingency Management. We hypothesize that the availability of an alternative reinforcer drives the subject into more Deliberative modes of decision making, which are more flexible and allow for the construction of valuation. This hypothesis predicts that, in the context of Contingency Management treatment, anything that is able to affect the construction of value will have a stronger influence on the subject's decision to not use drugs. We review modulating factors that can increase the effectiveness of Contingency Management, particularly those that improve and influence Deliberative decision-making systems (such as working memory and concreteness of options) that we argue will also have an influence on reducing drug consumption.
Conclusions: We propose that Contingency Management increases the subject's use of Deliberative decision-making processes, which compete with more automatic decision-making processes, such as Pavlovian and Procedural action selection, increasing the probability that a subject will choose the alternative reward over the drug reward.
Financial Support: This work was supported by NIH grants R01-DA024080 (ADR) and T32-DA007234 (PSR).

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DEPRESSION, NICOTINE WITHDRAWAL, AND SMOKING URGES IN SMOKING CESSATION.

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Aims: Nicotine withdrawal and urges have the potential for making smoking cessation more difficult. Depressed smokers may be disproportionately affected by withdrawal and urges, leading to greater difficulty in quitting. This study assessed whether elevated depression among 81 nicotine dependent smokers predicted changes in withdrawal and urges to smoke throughout smoking treatment.
Methods: Data were collected as part of a randomized trial comparing contingency management and standard smoking cessation. Two linear mixed model analyses were conducted. Withdrawal (Minnesota Nicotine Withdrawal Scale) and urge rating (Questionnaire of Smoking Urges) data from a baseline week and four treatment weeks were included as dependent variables. High and low depression scores were based on participant Beck Depression Inventory-II scores, and included as a fixed factor. Time-point was the within-subject factor.
Results: Depressed (N=18) and non-depressed participants (N=63) differed on age (p<.05), but no other demographic or smoking related variables (all p's >.05). The mixed model predicting changes in nicotine withdrawal revealed main effects for depression (p<.01) and time (p<.01). The mixed model predicting changes in smoking urges also revealed main effects for depression (p<.05) and time (p<.01), as well as a depression by time interaction (p<.05). Depressed smokers reported increased withdrawal and urges in the first week of treatment (following the baseline week) before reporting progressive reductions in withdrawal and urges, whereas non-depressed smokers reported consistent reductions in withdrawal and urges from baseline through the final treatment week.
Conclusions: Depressed and non-depressed smokers differed on patterns of withdrawal and urges to smoke, with those reporting depression showing increased withdrawal and urges when they initially reduced smoking.
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INCENTIVES IN PUBLIC ADDICTION TREATMENT PAYMENT SYSTEMS: INTENDED AND UNINTENDED EFFECTS.

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Aims: Innovative ways are needed to improve the quality of treatment for drug use disorders. Performance-based contracting (PBC) aims to align program incentives and purchaser goals, yet is uncommon in drug abuse treatment systems. In 2007, Maine implemented a second-generation PBC system with financial incentives, for outpatient programs, addressing problems identified with its previous PBC. This study aims to 1) Determine whether rewarded measures and outcomes changed under the PBC 2) Examine whether there was client selection due to the PBC 3) Explore possible unintended effects of the PBC.
Methods: We use state administrative data from 2005-2011 and multilevel modeling techniques with a difference-in-difference approach, and a non-PBC comparison group, to determine whether the 2007 PBC resulted in improved access and retention in treatment and whether positive or negative unintended effects stemmed from it.
Results: Preliminary analyses (N=25,105 admissions) indicated that the probability of receiving four or more outpatient treatment sessions did not change significantly between the 2005 – 2007 pre-period and the 2008 – 2011 post-period (OR .9, p =.16) and was not significantly different in the PBC agencies from the non-PBC agencies. Similarly there was no significant change in the probability of remaining in treatment for 90 days or more. The most significant predictors of retention were client characteristics (previous treatment, criminal justice involvement and homelessness). Client selection problems were not identified in an analysis of admission rates for individuals with diagnosed mental disorders. We continue to refine these models and examine the impact of the PBC on other factors and client outcomes.
Conclusions: Introduction of a PBC is a significant change in payment design that may affect how drug treatment services are delivered, thus increasing our understanding of its effects is critical. In preliminary analyses we find the overall net effect of incentivized contract very small and not significant.
Financial Support: NIDA R01 DA033402

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A COMPARISON OF DRUG-RELATED DEATHS IN FLORIDA, 2007–2012.

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Aims: The state of Florida maintains extensive and publicly available death records data tracking a variety of prescription and recreational drugs of abuse. The aim of this study was to examine the most frequently occurring drug-related deaths in Florida from 2007-2012.
Conclusions: Drug-related death data were obtained from the state of Florida for the years 2007-2012. The leading causes of drug-related deaths in Florida from 2007-2012 involved opioids and benzodiazepines. The Florida death data were sorted by the type of drug(s) involved in death: amphetamines, ethanol, benzodiazepines, inhalants, opioids or "other." Preliminary analyses examined specific drugs that were present at death including hydrocodone, oxycodone, alprazolam, and carisoprodol. Data were sorted to observe the numbers of deaths per year, and the number of deaths classified as "causal" or "present." Finally, we examined the number of deaths that occurred when each drug was used in combination with one or more other drugs. The majority of deaths occurred when Oxycodone and Hydrocodone were used in combination with at least one other substance. Alprazolam was the most common drug found in combination with hydrocodone or oxycodone.
Financial Support: N/A

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SEX AND DRUGS IN THE LIVES OF MINORITY WOMEN: A MULTI-LEVEL ANALYSIS OF SMARTPHONE-BASED DAILY DIARY DATA.

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Aims: Background: African American and Latina women are at increased risk of HIV infection through heterosexual contact. Daily smartphone-based diaries can provide event-level information about the context of sex and drug use behaviors that may help in our understanding of why heterosexual contact is so risky for minority women. The aim of this research was to investigate drug use and sex risk through the use of electronic daily diary collection methods.
Methods: Methods: 189 women were recruited into a smartphone daily diary study for a 12-week (84 days) diary period. Baseline interviews were completed and women consented to completing a data collection "app" using Samsung Android smartphones with unlimited text, Internet and voice capability provided by the study. Weekly incentives were provided for daily diary completion. Mplus was used for the multi-level analysis which specified a within-subjects process where we predicted that high-risk sex would occur on days on which women also used illicit drugs.
Results: Results: 140/189 women (74%) of the women completing the baseline interview consented to the daily diary study. Mean participation time was 62 days. The within subjects process was supported because days on which a woman reported receptive heterosexual anal intercourse with a male partner were also days on which she was more likely to also report vaginal intercourse (OR=3.65, CI 1.039,12.791), using methamphetamine (OR=1.90, CI 1.008,3.584), using cocaine (OR=4.46, CI 1.357,14.641), giving oral sex (OR=2.02, CI 1.016,4.032), receiving oral sex (OR=4.19, CI 1.889,9.287) and wanting sex (OR=1.39, CI 1.056,1.837).
Conclusions: Conclusion: This study identified predictors of daily anal intercourse that suggest that women may have problems moderating risky sexual behavior on days when they also engage in illicit drug use. Stimulant use was associated with positive mood (wanting to have sex) as well as multiple sexual behaviors in women.
Financial Support: California HIV Research Program grant ID10-CSULB-008 funded this project.

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COMBINING STRATEGIES: USING EVIDENCE-BASED INTERVENTIONS TO BUILD A MORE EFFECTIVE TREATMENT PROGRAM.

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Aims: We describe a new modification in our treatment program that addresses various psychological processes (craving, motivation, coping, emotional states, self-efficacy, outcome expectancies, interpersonal determinants) that may predict treatment outcomes. Although combined therapy effects may not be additive, they can provide incremental improvement in results. This proposal describes a strategy being developed at a community outpatient treatment program that combines several specific efficacious therapies during a single treatment episode.
Methods: Based on a dynamic model of relapse, our proposed treatment program implements several different treatments with positive outcomes. This approach combines pharmacotherapy, mindfulness-based interventions, and other therapies to address patient craving and improve meta-cognition, self-efficacy, and outcome expectancies. The program delivers a combination of frequently used evidence-based therapies including cognitive behavior therapy, motivational interviewing, twelve step facilitation, and multidimensional family interventions. Contextual-CBT interventions (Dialectical Behavior Therapy, Acceptance and Commitment Therapy, Mindfulness-Based Cognitive Therapy) are added in a deliberate consistent manner to increase psychological flexibility and patient coping (e.g. mindfulness, acceptance and defusion processes, emotional regulation, distress tolerance, and interpersonal effectiveness). This combination of these specific therapy components aims to address more completely the various factors mediating treatment outcomes.
Conclusions: Combining several typical psychotherapy strategies with pharmacotherapy and contextual-CBT interventions, under the supervision of an individual therapist and psychiatrist, will potentially increase patient motivation and improve treatment outcomes.
Financial Support: Linden Oaks Hospital at Edward

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EFFECTS OF AMYGDALAR CAMKII ACTIVITY ON EXTINCTION AND RECONSOLIDATION OF A COCAINE-ASSOCIATED MEMORY.

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Aims: The aims of our study were to determine the signaling cascades in the basolateral amygdala (BLA) that regulate the reconsolidation and extinction of cocaine-associated memories and whether manipulations of identified targets could inhibit reconsolidation or enhance extinction to reduce relapse-like behavior in an animal-model of addiction.
Methods: Rats trained to self-administer cocaine, paired with an audiovisual cue, underwent a test session in which the drug-cue memory was either reactivated by brief presentation to induce reconsolidation, or extinguished by multiple unreinforced presentations. Proteomic analysis was performed on BLA tissue to determine differentially expressed phospho-proteins following extinction and reconsolidation. In a second experiment, CaMKII, a target protein identified by proteomic analysis, was inhibited by infusion of KN-62 into the BLA immediately following memory reactivation or extinction. The effect of this inhibition was measured in a subsequent cue-induced reinstatement session.
Results: Proteomic analysis of tissue from the BLA revealed a decreased expression of pSer331 CamKIIα following memory reconsolidation and an increased expression following cue extinction. Furthermore, inhibition of CaMKII in the BLA via KN-62 resulted in decreased responding on a cue-induced reinstatement test both in rats that had undergone cue reactivation and in those in which the memory had been extinguished.
Conclusions: Phosphorylation of CaMKIIα, specifically at Ser331 may be differentially involved in the extinction and reconsolidation of a drug-induced memory. Additionally, intra-BLA infusion of KN-62, a specific CaMKII inhibitor, seems to impact these same memory processes. Therefore, CaMKII activity may be required for drug-memory reconsolidation, and inhibitors of CaMKII might be useful adjuncts to extinction-training in the treatment of addiction.
Financial Support: This research was supported by K01DA031745, The Pennsylvania Department of Health, and T32NS007433.

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BRIEF TOOLS FOR PEDIATRICIANS TO SCREEN 9- TO 12-YEAR-OLDS IN NEED OF PREVENTION FOR SUBSTANCE USE DISORDER.

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Aims: Healthcare-based prevention of substance use disorder (SUD) has been a policy for American Academy of Pediatrics for decades; the Affordable Care Act also supports such programs. Two previously-validated and computerized tools, parent-report Transmissible Liability Index (TLI) and child-report Risk Index (RI), will be acceptable to patients, their parents and pediatric staff and provide clinical utility when used during well child check-ups.
Methods: Following informed consent and child assent, while waiting for a physician in the exam room, parents and patients completed the TLI and RI, respectively. Nurses also invited parents to participate in a follow-up interview. Of 258 records scanned for eligibility (patients of 17 pediatricians within 3 practices), 106 parent-child dyads were recruited by nurses to complete the TLI and a RI prototype; 41.9% of patients were girls, 55.7% were African-American, 44.3% were Caucasian, and their mean age=10.3 years (SD=2.0).
Results: TLIs took a mean 5.3 minutes (range = 4.3-7.4); prototype RIs took a mean 5.1 minutes (range = 2.3-10.1). Parents and patients rated the screening protocol very positively. E.g., over 93% of parents reported they want pediatricians to use the screening tools; 96.6% reported that if the screening indicated their child needed prevention, they would seek help through a physician's referral. Pediatricians and office staff also viewed the protocol positively, patient flow was not disrupted, and medical staff agreed to assist in further development of a screening and referral protocol. Scores on both indexes correlated with substance use, conduct disorder, health behaviors that concern pediatricians (e.g., wearing a helmet while riding a bike) and many case-conceptualization measures used with the Family Check-Up prevention program.
Conclusions: The TLI/RI screening protocol fits pediatric well child check-up logistics, is acceptable, and provides clinical utility as a screening tool for healthcare-based SUD prevention.
Financial Support: Supported by grants from NIDA (P50 DA005605, R42 DA022127) and the Staunton Farm Foundation.

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EVALUATION OF THE ENVIRONMENTAL SUPPORT SCALE IN ADOLESCENCE.

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Aims: For some, the adolescent developmental period is marked by a steep increase in risk behaviors, including substance use. However, environmental sources of support have shown to modulate or buffer the effects of vulnerability to these outcomes. Despite the recognition of environmental support as protective, there exist few concise and valid assessments of this construct. The aim of this study was to explore the factor structure and validity of the Environmental Supports Scale (ESS; Tyler et al., 1991) in a diverse sample of adolescents.
Methods: A community sample of 246 adolescents (mean age = 13 years, 56.3% boys, 49.3% White, 35.5% African American) completed the ESS (15 items that assess positive relationships with adults and peers across multiple contexts) as well as measures of internalizing and externalizing symptomatology/behaviors for validation analyses.
Results: Principal axis factoring, with an oblique rotation, was conducted. An unconstrained exploratory factor analysis of the 15 items identified 3 eigenvalues greater than 1 (accounted for 36.87% of the total variance) and a natural break at the third factor. After rotation, a three-factor solution was retained and included a separate factor for Home, School, and Neighborhood. Convergent validation analyses revealed that the School and Neighborhood factors were negatively correlated with substance use [r = -.19 for both School (p = .003) and Neighborhood (p = .004)] as well as risk behavior (School r = -.31, p = .0001 and Neighborhood r = 1.17, p = .015). All three factors correlated negatively with depressive symptoms (r = -.26 to -.31, p = .0001 for all factors).
Conclusions: A brief assessment of perceived support in specific contexts fills an important gap in the resilience processes literature. The ESS captures what is similar across developmental contexts (positive relationships) while also providing a tool to examine the unique impact of each context on substance use and other risk behaviors.
Financial Support: NIDA Grant R01 DA018647-08

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FACTORS ASSOCIATED WITH INTERNALIZED INJECTION DRUG USER STIGMA AMONG INJECTION DRUG USERS IN NEW YORK CITY.

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Aims: Little is known on the effect of injection drug user (IDU) discrimination and stigma on the health and risk behaviors of IDUs. IDUs may internalize these negative attitudes and experiences and stigmatize themselves (internalized stigma) and/or impose these negative feelings on others. With previous research suggesting the harmful effect of internalized stigma and discrimination on behavior, we aim to determine sociodemographic, and sex and drug use risk behaviors associated with having stigmatizing attitudes towards IDUs among a sample of IDUs in New York City.
Methods: Participants were recruited from 3 pharmacies located in high drug activity neighborhoods and were regular pharmacy customers, IDU syringe customers, or recruited peers of IDU syringe customers and completed a survey on risk behaviors, access to services, and IDU stigma. Among IDUs (n=143), GEE was used to account for clustering of IDU peers and to examine factors associated with higher IDU stigma score.
Results: IDUs were mostly Hispanic/Latino (54.6%), male (78.3%) with a mean age of 42.7 years. Those with higher IDU stigma scores were more likely to be Latino compared to White (AOR=1.42, 95% CI:1.10-1.85) and less likely to have a high school level education (AOR=0.61, 95% CI:0.47-0.49), lend a syringe in the past 3 months (AOR=0.75, 95% CI:0.57-0.97), and use a sterile syringe source in the past 3 months (AOR=0.53, 95% CI:0.29-1.00).
Conclusions: These data suggest that while IDUs with higher internalized IDU stigma may refrain from lending their syringe to someone else perhaps due to negative feelings toward drug use, they are less likely to acquire a sterile syringe increasing their personal risk of HIV and other blood-borne infection. Stigmatizing attitudes may translate into feelings of discomfort or shame in patronization of public syringe access venues and provides additional evidence supporting the need for HIV prevention interventions addressing stigma.
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STIGMATIZING EXPERIENCES WHILE IN DRUG ABUSE TREATMENT: A QUALITATIVE EXPLORATION OF CLIENT'S PERCEPTIONS.

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Aims: Stigma involves disapproval and discrimination of individuals bearing a discrediting mark. Drug abuse is a widely stigmatized condition for which treatment involves a great degree of social control. Although social distancing has been documented in mental health treatment settings, less is known about the effect of stigma in the drug abuse treatment sector. We explore client's perceptions of practices during treatment that may contribute to stereotyping and discrimination in ways that affect therapeutic alliance, client's well-being and self-esteem, and enhance the risk of treatment abandonment. Findings will inform theory construction and subsequent research to mitigate stigma among providers.
Methods: In-depth semi structured individual interviews and focus groups were performed with purposeful sample of 16 clients in a public Methadone Maintenance Treatment program in Puerto Rico. An interview guide was designed to explore barriers and facilitators to treatment retention. Grounded theory methods were used to systematically identify and classify text content, to generate a codes list, and to interpret qualitative data of individuals' previous drug treatment experiences. Data analysis was developed as an iterative process by a panel of 3 judges to minimize bias or selective inattention. Data files were managed using ATLAS.ti.
Results: Mean age was 41 years, 32% were female, and 94% had completed a high school degree or greater. All had been previously in drug treatment more than once. Multiple factors affecting treatment entry and retention were identified. Participants described experiences that they construed as degrading, humiliating, and abusive. Many of the confrontational interventions carried out by staff to "help" clients overcome their drug problem were identified as barriers to retention. Human rights issues are questioned.
Conclusions: Clients' perspectives need to inform research on stigma in the drug treatment sector. Barriers and facilitators reflective of stigma need to be addressed to facilitate client centered care under a chronic care model.
Financial Support: NIDA Grant #1R24DA024868-01A2

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CAFFEINE AND ALCOHOL INTAKE AND NICOTINE DEPENDENCE SEVERITY IN FEMALE SMOKERS.

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Aims: The co-administration of other psychoactive compounds with cigarettes may have implications for tobacco-related health outcomes. Smokers are more likely than non-smokers to consume caffeine and alcohol, and nicotine dependent smokers tend to consume more caffeine and alcohol than non-dependent smokers, but few studies have explored the relationships between severity of nicotine dependence and frequency of caffeine and alcohol use among established daily smokers.
Methods: During baseline assessment, 122 nicotine dependent women enrolled in a smoking cessation study recorded alcohol and caffeine use using the Smoking History Survey, and completed the Fagerström Test for Nicotine Dependence (FTND) to assess severity of nicotine dependence. Spearman correlations were used to assess the relationships between FTND score and alcohol and caffeine consumption.
Results: Analysis revealed a significant positive correlation between caffeine intake and FTND score ($r=-0.366$, $p<0.0001$) but a significant negative correlation between weekly alcohol use and FTND score ($r=0.272$, $p=0.002$).
Conclusions: These findings suggest that the positive relationship between cigarette smoking and caffeine consumption, previously reported in smokers versus nonsmokers and dependent versus non-dependent smokers, extends to established nicotine dependent smokers. In contrast, alcohol consumption may have a more complex relationship with cigarette smoking. While smokers versus nonsmokers and dependent versus non-dependent smokers are more likely to consume alcohol, severity of nicotine dependence among established smokers is negatively correlated with alcohol use in the present sample. It may be that highly dependent smokers have crossed a threshold, beyond which alcohol plays a diminished role in maintenance of smoking.
Financial Support: This research was supported by National Institute on Drug Abuse grants P50DA16511 and R25DA020537.

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ATTENTIONAL BIAS TO ALCOHOL-RELATED STIMULI AND THE SELF-REPORTED DESIRE TO DRINK FOLLOWING A DOSE OF ALCOHOL.

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Aims: Moderate and heavy alcohol users tend to allocate their attention in favor of cues associated with alcohol. This attentional bias (AB) may be an indication of motivation to consume alcohol that could trigger alcohol use. As an implicit cognitive process, AB may contribute to alcohol use even when drinkers do not report conscious desire to drink. We examined two aspects of AB towards alcohol-related cues. First, we examined how AB changes after drinkers consume alcohol. Second, we tested whether AB was associated with participants' explicit self-reports of their desire for alcohol.
Methods: A visual-probe task measured AB to alcohol images under two alcohol doses: a placebo and 0.64 g/kg abs. alcohol. As an explicit measure of motivation to drink, participants self-reported their desire for alcohol on a visual analogue scale. Following 0.64 g/kg alcohol, both measures were administered twice: once as BAC ascended and again as BAC began to descend. The measures were administered at the same times following placebo.
Results: Participants showed AB following placebo. Following the active alcohol dose AB was reduced during the ascending limb but returned during the descending limb. Conversely, subjective desire increased initially during the ascending limb of the active dose but not during the descending limb. There were no significant correlations between participants' AB and subjective desire for alcohol during any test.
Conclusions: The decreased AB observed early after drinking, as BAC rises, suggests reduced motivation to drink, possibly due to satiation from receiving the active dose. However, this satiation was brief as AB quickly returned as BAC began to descend. Changes in AB failed to correspond with changes in self-reported desire to drink, suggesting independence between these two indicators of motivation for alcohol. This is consistent with the idea that AB represents a mechanism underlying the motivation to drink that is implicit and not at the drinkers' level of conscious awareness.
Financial Support: Research supported by NIAAA grant 018274 and NIDA grant 035200.

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STRIATAL DOPAMINE D2/3 RECEPTORS IN METHAMPHETAMINE USERS: RECOVERY WITH EXERCISE AND ABSTINENCE.

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Aims: Methamphetamine (MA) dependence is associated with deficits in markers for striatal dopamine (DA) signaling (Lee et al., 2009), and striatal D2/3 DA receptor availability (binding potential, BP_{ND}) predicts success of behavioral treatments for this disorder (Wang et al., 2012). Therefore, manipulations that augment DA signaling may ameliorate neurobehavioral deficiencies in MA dependence. Treadmill exercise increases DA D2/3 receptor expression (Gilliam et al., 1984) and reduces MA-induced damage to DA neurons (O'Dell et al., 2012) in rodents. Exercise also increases D2/3 BP_{ND} in Parkinson's disease patients (Fisher et al., 2012). In addition, neuroprotective effects of exercise on DA cells depend upon brain derived neurotrophic factor (BDNF) (Gerecke et al., 2012). Here, we tested the effects of exercise on D2/3 receptor BP_{ND} and BDNF levels in MA users who maintained abstinence while receiving behavioral therapy in a residential program.
Methods: Treatment-seeking MA users were randomized to two groups: Exercise (EX n=10) or Education (ED n=8), and underwent supervised exercise training or attended health education classes 3d/wk for 8 wks, respectively. Before and after the interventions, subjects underwent [18F]fallypride PET imaging to assay D2/3 BP_{ND} and blood sampling to measure serum BDNF (n=7). Healthy subjects (HC n=23) who underwent one PET scan were included for comparison.
Results: Both of the MA groups had 15% lower BP_{ND} than HC ($p<0.05$). After the intervention, BP_{ND} was increased in EX subjects (14% $p<0.01$) but not in ED subjects. The EX group, but not the ED group, showed normalization of BP_{ND} to HC levels and a decrease ($p<0.01$) in serum BDNF levels.
Conclusions: Increases in D2/3 BP_{ND} in MA users may reflect an exercise-induced augmentation of DA signaling. Clinical implications of these results support adding an exercise regimen as a potential adjunctive treatment for stimulant dependence.
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DIFFERENCES BETWEEN HEROIN AND NON-PRESCRIPTION OPIOID ANALGESICS USERS IN TREATMENT-SEEKING OPIOID-DEPENDENT YOUNG ADULTS.

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Aims: The purpose of this study was to evaluate the demographic, infectious disease status and clinical severity of dependence among heroin users compared to non-prescribed opioid analgesic users in a group of opioid dependent young adults seeking treatment with buprenorphine/naloxone.
Methods: 124 young adults with opioid dependence that were seeking medication-assisted treatment with buprenorphine/naloxone were compared on their primary opioid of use. Demographic variables with assessments that included rapid HIV screening, Hepatitis C, severity of opioid use, ASI composite scores, SDS, COWS, opioid craving scale, and CES-D were collected. The main data analyses were performed using independent t-test and chi-square.
Results: The participants were predominately male (64.5%) with an age ranging between 18 to 25 years ($m = 22.6$; $sd=1.9$), Caucasian (92%), graduates from high school (GED included) or had some college (79%), less than half were unemployed, most were never married (94%) and all had used opioids for 3.5 years. The heroin subgroup (n=30) were predominately IVDU (86.7%) whereas the opioid analgesics users (n=94) were less likely to but still used IV (6.5%) ($p < 0.0001$). None of the subjects tested positive for HIV and only two participants were already aware of their positive status for hepatitis C. The heroin group was more likely to use other opioids as the secondary drug of abuse, and the opioid analgesic group more likely to used cannabis ($p < 0.0001$). The heroin subgroup scored significantly higher on psychiatric ASI composite score relative to the opioid analgesic users ($p = 0.006$).
Conclusions: The majority of young adults were dependent on opioid analgesic, and those who were dependent on heroin were more likely to use IV but none of the participants tested positive for HIV and only two had hepatitis C. The heroin subgroup had higher score on ASI psychiatry suggesting that this group may need additional evaluation and treatment.
Financial Support: Supported by NIDA grant R01DA027138 (GG).

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FISCAL: AN ALL-DATA APPROACH TO ASSESSING FINANCIAL CAPABILITY IN PEOPLE WITH PSYCHIATRIC DISABILITIES AND SUBSTANCE USE.

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Aims: The goal of this project was to develop a more effective, reliable, and evidence-based method to assess the ability of disabled persons to manage federal disability payments without a representative payee or other fiduciary. This paper describes the development of the FISCAL (Financial Incapability Structured Clinical Assessment done Longitudinally) measure of financial capability.
Methods: The FISCAL was developed by an iterative process of literature review, pilot testing, and expert consultation. Independent assessors used the FISCAL to rate the financial capability of 118 people who received Social Security disability payments, had recently been in acute care facilities for psychiatric disorders, and who did not have representative payees or conservators. The instrument's psychometric properties, inter-rater reliability, and agreement with other measures were then assessed.
Results: Altogether, 48% of participants were determined financially incapable by the FISCAL, of whom 60% were incapable due to unmet basic needs, 91% were incapable due to spending that harmed them (e.g. on illicit drugs or alcohol), 56% were incapable due to both unmet needs and harmful spending, and 5% were incapable due to contextual factors. As expected, incapable individuals had been hospitalized significantly more often for psychological problems ($p<.05$) and scored higher on a measure of money mismanagement ($p<.001$) than capable individuals. Inter-rater reliability for FISCAL capability determinations was good (Kappa=.731) and inter-rater agreement was 89%.
Conclusions: The FISCAL has construct validity as a measure of financial incapability, demonstrated good reliability, and correlated with related measures. It can be used to validate other measures of capability and to help understand how people on limited incomes manage their funds.
Financial Support: This research was supported by grants from the National Institutes of Health (R01DA025613 and R01DA12952).

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COMPARISON OF ADOLESCENT SELF-REPORTS OF THE NONMEDICAL USE OF SCHEDULED PRESCRIPTION MEDICATIONS IN SELF-ADMINISTERED SURVEYS VS. SEMI-STRUCTURED INTERVIEWS.

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Aims: To compare self-reports of nonmedical controlled prescription drug use in adolescents (viz., using someone else's medication) using self-administered web-based surveys and semi-structured interviews.
Methods: A longitudinal study employing both annual web-based surveys and face-to-face interviews every 6 months was conducted with 544 adolescents between 2009 and 2013. Every year of the survey and at least 6 waves of interviews were completed by 401 of the adolescents. This study focuses on one survey and the corresponding interviews in 2012 and 2013. SAMPLE: The sample included 401 males (50.6%) and females (49.4%) who were in either the 10th (48.6%) or 11th (51.4%) grade in 2012/2013. The sample was 77% White, 17.5% African-American, and 5.2% from other ethnic groups.
Results: The analysis revealed low correspondence between the survey and the interviews on variables indicating past-year nonmedical use of opioids ($K=.309$, $p<.001$), stimulants ($K=.266$, $p<.001$), anxiolytics ($K=.123$, $p<.001$), and sedatives ($K=.157$, $p<.001$). Among all past-year nonmedical users in either the survey or the interviews (n=37), 21.6% showed perfect agreement between the two modes of data collection, while 18.9% indicated nonmedical use only in the interviews, and 59.5% indicated nonmedical use only in the survey.
Conclusions: Although our findings support past research which suggests respondents are more likely to report sensitive information on web-based self-administered surveys as compared to interviews, both modes of data collection measuring nonmedical use of prescription drugs appear to miss a substantial segment of adolescents who engage in this type of behavior. Further, given that a smaller percent of adolescents acknowledged nonmedical use via interview (particularly the use of anxiolytics and sedatives), researchers may need to evaluate how best to approach this issue when collecting sensitive information using qualitative methods.
Financial Support: This research was supported by research grants R01DA024678, R01DA031160, T32DA007267.

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DOES MARIJUANA INCREASE RISK FOR DATING VIOLENCE VICTIMIZATION OR PERPETRATION?: RESULTS OF A META-ANALYSIS.

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Aims: To conduct a meta-analysis of results published in that past decade that address the question: "Is marijuana use associated with either DV victimization or perpetration?"
Methods: Studies were included if published between 2003-2013 in a peer-reviewed journal and reported a measure of association between DV and marijuana use for U.S. youth who were between the ages of 11-25 years old. PRISMA guidelines were followed. A total of 444 abstracts were screened, 41 included in a synthesis of results, and 9 in the meta-analysis. A sole study may have presented separate measures for males and females. All measures of association were converted to odds ratios (ORs) in order to calculate combined ORs.
Results: Using 12 ORs, the combined OR for the association between DV victimization and marijuana was 1.43 (95% CI: 1.30-1.57). The association remained after correcting for publication bias and using both fixed and random effects weighting. The association was stronger for females than for males. Using 4 estimates, the combined OR for the association between DV perpetration and marijuana was 1.28 (95% CI: 1.09-1.50). Concerns about the methodologies of the underlying studies, and the small number of studies, suggest the true effect of marijuana use on perpetration is not yet able to be identified. It is noted that the arguably most rigorous paper found a protective effect of marijuana use against DV perpetration (see Temple 2013).
Conclusions: The existing evidence supports the contention that marijuana use by youth is associated with DV victimization, though there are too few results available to make conclusions about the relationship between marijuana use and perpetration. It is not clear that marijuana use is causally associated with victimization, and may be attributable to confounding factors. Additional research on DV perpetration and marijuana is needed.
Financial Support: NIAAA K01AA017630

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LONG-TERM COCAINE SELF-ADMINISTRATION IN FEMALE CYNOMOLGUS MONKEYS: CHANGES IN BEHAVIOR AND IN DOPAMINE TRANSPORTERS AND D2-LIKE RECEPTOR AVAILABILITY.

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Aims: Previous studies in male monkeys have shown that over 1 year of cocaine self-administration (SA): (1) intake does not increase; (2) tolerance does not develop to the rate-decreasing effects of cocaine; and (3) dopamine (DA) D2-like receptor availability shows dose-dependent reductions. There is accumulating evidence of sex differences in cocaine abuse, including greater vulnerability in initiating drug use and more adverse consequences of abuse in women compared to men. In monkeys, there appears to be sex differences in the relationship between cocaine SA and baseline D2-like and DA transporter (DAT) availability. Thus, the goal of the present study was to extend the earlier work done in male monkeys to female monkeys.
Methods: Baseline PET scans were obtained in female cynomolgus monkeys (n=10) using the D2-like receptor ligand [11C]raclopride and the DAT ligand [18F]FECNT. Next, all monkeys were trained to respond under a multiple fixed-interval 3-min schedule of food and cocaine reinforcement. Food was available in components 1 and 3 and cocaine (0.2 mg/kg/inj) in components 2 and 4.
Results: There were no significant relationships between baseline D2-like and DAT availability and rates of cocaine SA. Long-term (3-12 months) cocaine SA resulted in decreases in D2-like receptor availability and increases in DAT availability. Preliminary data suggest that DAT availability increased following 100 mg/kg and then declined back to baseline levels with continued cocaine SA (1000 mg/kg). Unlike what was reported in males, it appears that continued exposure to cocaine results in increases in intake and tolerance developing to the rate-decreasing effects on food-maintained responding.
Conclusions: These studies suggest sex differences in behavior maintained by cocaine and in the consequences of long-term cocaine SA on DA receptor function.
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SMOKING CRACK MIGHT INCREASE HIGH RISK INJECTION PRACTICES AMONG PEOPLE WHO INJECT DRUGS.

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Aims: To examine the relationship between high risk injection practices and crack smoking among PWID.
Methods: Analyses were carried out on the Montréal subsample of the ongoing eastern Canada SurvUDI surveillance system database. Participants are people who injected recently (past 6 months). They are recruited mainly in harm reduction programs. Each visit includes a structured interview and the collection of saliva for anti-HIV and anti-HCV antibody testing. Using GEE methods, a model was created for each risk practice, controlling for socio-demographic characteristics (age, sex, residential status, education level), age of first injection and types of drugs injected (cocaine, speedball/heroin and prescription opioids) as required. Adjusted prevalence ratios (aPR) were calculated and 95% Wald confidence interval (CI) were estimated.
Results: Of the 2300 PWID recruited between 2004 and 2012, (79.2% males; mean age: 36.4 years; 4792 visits), 68.7% had recently smoked crack at their first visit; main drug of injection was cocaine powder (61%). Compared to PWID who did not smoke crack, PWID who smoked crack were more likely to inject with someone else (aPR = 1.17, CI: [1.11-1.24]) and use injection material used by someone else such as syringes (aPR = 1.23, IC: [1.05-1.44]), water (aPR = 1.27, CI: [1.09-1.49]), filters (aPR = 1.42, CI: [1.14-1.78]) and cookers (aPR= 1.37, CI: [1.16-1.62]). No significant associations were found for injection in public (aPR = 1.03, CI: [0.98-1.09]) and daily injection (aPR = 0.91, CI: [0.82-1.00]).
Conclusions: Although powder cocaine is the main drug injected by most Montréal PWID, crack smoking is unexpectedly highly prevalent among them. This study is one of the few showing an association between crack smoking and high risk injection practices, mostly the sharing of injection material, among PWID.
Financial Support: Health Canada and Québec Ministry of Health

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RACIAL/ETHNIC DIFFERENCES IN ATTENTIONAL BIAS AND CUE REACTIVITY AMONG INDIVIDUALS WITH MARIJUANA USE DISORDERS.

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Aims: This study examines cognitive and psychological factors associated with attentional bias and cue reactivity among individuals with marijuana use disorders and whether race/ethnicity moderates these associations.
Methods: Six participants with marijuana use disorders and six healthy controls matched on race, age, gender, and education completed a novel laboratory based experimental task designed to assess marijuana cue-reactivity and inhibitory control. Participants completed a visual attention task (a modified Eriksen Flanker task) where they were shown a series of three lines (one after the other) and asked to respond to the orientation (vertical or horizontal) of the second (target) line. The flankers (first and last lines) were identical to each other and either matched (congruent trial) or did not match (incongruent trial) the target in orientation. Neutral, emotional (positive and negative), and marijuana-related images were superimposed on the target. During performance of this task, physiological recordings were made of the their Event Related Potentials (ERPs), Galvanic Skin Response (GSR), and Heart Rate (HR). Behavioral data (reaction time and accuracy) were also gathered.
Results: Preliminary data analysis revealed that, compared to healthy controls, marijuana users showed an overall slower reaction time to all images (neutral, positive, negative, marijuana), which reflects a general attentional breakdown. Moreover, marijuana users suffered more interference and reduced reaction time in response to incongruent trials when distracted by the marijuana and neutral images than for any other images. There were no significant racial/ethnic differences in these preliminary analyses.
Conclusions: The attentional deficits we see among marijuana users may be a consequence of chronic marijuana use or a pre-existing condition that influences the development of their addiction. Implications for the development of interventions designed to reduce the consequences of marijuana use will be highlighted.
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INFLUENCE OF BUSPIRONE ON THE CARDIOVASCULAR AND SUBJECT-RATED EFFECTS OF METHAMPHETAMINE.

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Aims: Preclinical data indicate that pretreatment with buspirone, a non-benzodiazepine anxiolytic, reduces the abuse-related effects of methamphetamine, suggesting it may be an effective antagonist pharmacotherapy. This study sought to translate preclinical findings to the human laboratory by examining the effects of methamphetamine when combined with buspirone.
Methods: Ten subjects reporting recent illicit stimulant use completed a placebo-controlled, crossover, double-blind protocol in which the effects of oral methamphetamine (0, 15 and 30 mg) combined with acutely administered oral buspirone (0 and 30 mg) were determined. During each session, subjects completed a battery of physiological and subject-rated measures. Data were analyzed using repeated-measure ANOVA, followed by a priori planned comparisons with the hypothesis that buspirone would attenuate the stimulant-like effects of methamphetamine.
Results: Methamphetamine produced prototypical stimulant-like cardiovascular and subject-rated effects (e.g., elevated blood pressure; increased ratings of End-of-Day ratings Good Effects). Buspirone alone was generally devoid of effects. Buspirone attenuated the cardiovascular effects of methamphetamine and enhanced a number of abuse-related subject-rated effects (e.g., End-of-Day ratings of Good Effects).
Conclusions: Future research should examine the effects of chronic buspirone dosing to better determine it clinical usefulness more managing methamphetamine dependence, however.
Financial Support: Supported by grants from NIDA (R01 DA025032 and R01 DA025591) to CRR.

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FAMILY ENVIRONMENT AS A MEDIATOR OF RELATIONS BETWEEN FAMILIAL RISK AND IMPULSIVITY.

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Aims: To examine family environment as a mediator of relations between familial risk and impulsivity at study entry and again after 6 months.
Methods: Preadolescents (ages 10-12 at baseline) who have not initiated substance use with (FH+; n = 283) and without (FH-; n =78) family history of substance use disorder and their parents were recruited from the community. Linear regression analyses were conducted to test if family environment (Family Assessment Measure, parent and youth overall score standardized and averaged) mediated relations between family history (yes/no) and impulsivity (Barratt Impulsiveness Scale-11 total score). The Sobel test was used to assess statistical significance. Analyses controlled the effects of age.
Results: At baseline and at 6 months, we predicted an increase in BIS-11 total score due to the direct effects of FH status (p<.001). FH+ status was associated with an increase in BIS-11 total score through family environment (p<.001), indicating family environment mediated relations between familial risk and impulsivity at baseline and again after 6 months. Both mediation models were significant (p <.001).
Conclusions: Results show that FH+ youth have higher rates of impulsivity if they have a dysfunctional family environment. Results support familial relationships as important for shaping self-control. These results highlight the importance of prevention and intervention services designed to target parenting and family systems, especially among families with a history of substance use disorder. Tests of these relations are underway using Structural Equation Modeling. By May, many of these youth will have initiated substance use. We will add this outcome to test the impact of this mediation model on substance use initiation.
Financial Support: R01-DA026868, R01-DA033997, R01-DA033997-02S2

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CHARACTERIZATION OF THE DISCRIMINATIVE STIMULUS EFFECTS OF THE NOP AGONIST RO 64-6198 IN NON-HUMAN PRIMATES.

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Aims: The NOP receptor is the most recently identified member of the opioid receptor family (Mollereau et. al. 1994). In non-human primates, NOP agonists produce potent analgesia without the side effects associated with mu opioid receptor (MOR) agonists such as itch, respiratory depression, and abuse liability (Ko et al. 2009). However, the ability of NOP agonists to produce interoceptive effects, and the degree to which these effects are receptor mediated, has not been evaluated. This study aims to characterize the interoceptive properties of the small molecule NOP agonist Ro 64-6198.
Methods: Rhesus monkeys were trained to discriminate Ro 64-6198 0.18 mg/kg (n=2) or 0.1 mg/kg (n=1) from saline. Another group of animals was trained to discriminate fentanyl 0.01 mg/kg from saline (n=3).
Results: Both Ro 64-6198 and fentanyl produced dose-dependent discriminative stimulus effects. In tests of drug generalization, fentanyl did not substitute for the training dose of Ro 64-6198 in animals trained to discriminate Ro 64-6198. Likewise, in fentanyl-trained animals, Ro 64-6198 did not generalize to a fentanyl cue. The training dose of Ro 64-6198 was blocked by J-113397, a selective antagonist for the NOP receptor, but was not antagonized by a MOR selective dose of naltrexone. In contrast, the training dose of fentanyl was blocked by a MOR selective dose of naltrexone but not by J-113397. Substitution studies with diazepam indicate that doses between 3-10 mg/kg produce partial to full generalization in animals trained to discriminate Ro 64-6198. Diazepam did not produce generalization in fentanyl-trained animals.
Conclusions: Preliminary data show that the NOP receptor agonist Ro 64-6198 does not share interoceptive properties with the MOR agonist fentanyl. These effects appear to be receptor mediated. Interestingly, diazepam produced partial to full generalization in Ro 64-6198 trained animals suggesting that NOP agonists and benzodiazepines may share interoceptive properties. Future studies will continue to evaluate these effects.
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UNODC-WHO PROGRAM ON DRUG DEPENDENCE TREATMENT AND CARE: BUILDING TREATMENT CAPACITY IN LOW AND MIDDLE INCOME COUNTRIES.

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Aims: The UNODC-WHO Programme on Drug Dependence Treatment and Care was launched in 2009. The overall aim of the UNODC-WHO Programme is to promote and support worldwide (with a particular focus on low- and middle income countries), evidence-based policies, strategies and interventions that are based on a public health and human rights approach, in order to reduce drug use and the negative health and social consequences associated with it.
The UNODC-WHO Programme follows four synergic lines of action at the national level, including: drug treatment-related research; the development and strengthening of treatment services; advocacy related activities; and capacity building on evidence-based drug dependence treatment and care. The UNODC-WHO Programme on Drug Dependence Treatment and Care has been implemented in a range of countries in South East Europe, Latin America and the Caribbean, Sub-Saharan Africa, West Asia and South East Asia. Capacity building includes training, which is delivered at the regional and the national level as well as sharing of good practices, mentoring and mutual learning.
The poster will present capacity building outcomes of the UNODC-WHO Programme as well as opportunities for research collaborations.
Conclusions: The effective treatment of drug dependence is of significant public health importance. Through this joint programme, UNODC and WHO have strengthened their collaboration on drug dependence treatment and care at the global, regional and national levels.
The capacity building component of the UNODC-WHO Programme shows an increase in knowledge from pre-assessment to post-assessment (in the trainings), and an overall positive effect with regard to knowledge transfer to the practitioners at the national level.
Financial Support: We thank our donors: France, Italy, Sweden, the United Arab Emirates and the United States of America.

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PREFERENCE AND C-FOS ACTIVATION OF DRUG REWARD VS. NATURAL REWARD: ARE FEMALE PHEROMONES MORE REWARDING THAN COCAINE?

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Aims: Drugs of abuse and natural reinforcers both activate neural structures that regulate motivational behavior and the perception of reward. Cocaine (Coc) is a strong psychomotor stimulant and female pheromones (Phe) increase dopamine in neural structures involved in sex and reward. The objective of this experiment is to determine (1) whether a clear preference to Coc or Phe can be established and (2) whether Coc activates the same neural structures when compared to Phe.
Methods: Behavioral preference was determined using conditioned place preference (CPP) in adult sexually naive males to determine whether a preference was acquired to Coc, Phe and what happens when both stimuli are presented. One hour after the CPP they perfused and stained for c-fos by immunocytochemistry. The nucleus accumbens (NAC) and medial preoptic area (MPOA) were analyzed. Pictures were taken using a light microscope at 10X magnification using the rat brain atlas and the NIH program Image J to determined a threshold of for the immunopositive cells and area.
Results: Male rats (n=6/group) displayed a preference for Coc and Phe; however, when given a choice between either stimulus, no clear preference was observed in the CPP task. As for the neuronal activity, Phe elicit the highest fos activation in both the NAC and MPOA. Surprisingly, the animals exposed to Coc and Phe had significantly less c-fos-ir when compared to cocaine and pheromone groups in the MPOA.
Conclusions: These data suggest that both the NAC and MPOA are involved in the natural reward and drug reward pathways. However, when both stimuli are presented, there less activation of these neural structures which results in the inability to identify a stimulus preference. Further studies will address what could be regulation the activation of these neural structures.
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INTEGRATED TREATMENT FOR MOTHERS INVOLVED IN CHILD WELFARE FOR SUBSTANCE ABUSE.

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Aims: Aims: Only 10-22% of mothers involved in the CWS complete SUD treatment. CWS involved families are referred to multiple services including parenting classes and ancillary services (e.g., housing, employment). Competing provider schedules and low resources contribute to low treatment completion. This pilot study aimed to determine the feasibility and efficacy of an integrated treatment for mothers involved in the CWS for SUD.
Methods: Methods: Drawing on evidence-based behavioral strategies, an intensive community-based treatment was developed (i.e., FAIR). Mothers (n = 31) involved in the CWS for hard substance use (94% methamphetamine; 6% opiates; 45% IV users; 7% HIV positive) and neglect were referred. Sessions involved frequent urinalysis, an individually tailored reinforcement system, parent training, 24/7 support, assistance with ancillary needs (mental health, housing, employment), and an integrated framework of the interplay between substance use and parenting. Additional supports included skills coaching for children, couples treatment, and a Resource Builder who created a "FAIR store" of incentives.
Results: Results: Outcomes indicated that the majority of mothers randomized to FAIR (13 TAU; 18 FAIR) engaged in (94%) and completed treatment (87%), showing significant reductions in substance use and cravings, and in psychosocial correlates (e.g., depression and trauma symptoms). They showed significant improvements in parenting and substance use correlates including parental stress, child abuse potential, and stability (housing, employment). Significant relationships showed that as substance use decreased, so did problematic symptoms.
Conclusions: Conclusions: Mothers involved in the CWS for co-occurring SUD and child neglect will successfully engage in treatment when individualized incentives and engagement strategies are provided. Once engaged, the majority of mothers completed treatment and demonstrated reductions in substance use and improvements in areas necessary for successful parenting. Discussion will focus on lessons learned to inform a larger randomized clinical trial.
Financial Support: Support: NIDA K23DA021603; P30DA023920

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WITHDRAWN

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HEPATITIS C VIRUS TESTING AND TREATMENT AMONG HIV-INFECTED PEOPLE WHO INJECT DRUGS IN ST. PETERSBURG, RUSSIA.

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Aims: The HIV epidemic in the Russian Federation, driven by injection drug use, is among the fastest growing in the world. Hepatitis C virus (HCV) infection is highly prevalent among people who inject drugs (PWID). Although treatment for HCV has been low among PWID, with newer therapies it may become possible to provide treatment to prevent complications and reduce transmission in this population. The study aim was to describe the current frequency of HCV testing and treatment in a cohort of HIV-infected PWID in St. Petersburg Russia.
Methods: This study used baseline data from the "Linking Infectious and Narcology Care" (LINC) study, a randomized controlled trial of an intervention to link HIV-infected PWID hospitalized at a narcology hospital with HIV medical care. Participants were 18-70 years old, HIV-infected, and had a history of injection drug use. Descriptive statistics were performed to assess the frequency of HCV screening and treatment.
Results: Participants (n=263) had a mean age 33.7 (SD±4.9) years, 26% female, 100% Caucasian, 54% unemployed and 14% married/partnered. Median years since HIV diagnosis was 6.3 (IQR: 4 -11). Median CD4 cell count was 315 (IQR: 161 - 491) and only 5.3% had ever been on anti-retroviral therapy. In the past month, 86% had used heroin and 23% reported sharing works. Nearly all participants had been screened for HCV (259/263; 98.5%), and all screened reported that they were positive. Only 4 participants (2%) reported ever receiving HCV treatment.
Conclusions: Among HIV-infected PWID hospitalized for opioid dependence in St. Petersburg, Russia, nearly all reported being screened for HCV and testing positive, while only 2% had received treatment. Substantial opportunities exist in narcology hospitals for eradicating HCV in HIV-infected Russian IDUs.
Financial Support: NIDA R01DA032082

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RACE AND ETHNICITY DIFFERENCES AMONG ADULTS WITH STIMULANT USE DISORDERS IN A RESIDENTIAL TREATMENT SETTING: A BASELINE ANALYSIS OF THE STRIDE COHORT.

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Aims: To compare racial and ethnic groups on baseline measures of stimulant and other drug use patterns, clinical features, co-morbid medical disorders, legal status, quality of life, and daily functioning among cocaine and stimulant abusing/dependent patients in a residential treatment setting.
Methods: Baseline data from a multi-site randomized clinical trial of vigorous exercise as a treatment strategy for stimulant abuse or dependence were analyzed. Participants (N=290) were 115 females and 175 males recruited from 9 drug treatment programs. The diverse sample included Blacks (n=128), Hispanics (n=31) and Whites (n=131). Assessments included self-reported drug, alcohol, and nicotine quantity and frequency, physical and mental health functioning, well-being and quality of life.
Results: Significant differences between racial and ethnic groups were found on drug use characteristics and stimulant use disorders. Blacks (97.7%) had higher rates of cocaine use versus Whites (63.4%) or Hispanics (67.7%), $p < .001$, but lower rates of methamphetamine use (3.1%) than Hispanics (35.5%) and Whites (47.3%), $p < .001$. On measures of mental health, Black participants endorsed fewer psychiatric disorders, $p = 0.002$, and symptoms of depression than Whites or Hispanics, $p < 0.001$, and also reported a lower risk for suicide, $p = 0.008$, than Whites. Black participants self-reported poorer physical health status and lower physical and cognitive functioning than Whites.
Conclusions: Findings highlight the importance of integrating health and mental health services into substance abuse treatment and could help identify potential areas for intervention to improve treatment outcomes for racial and ethnic minority groups.
Financial Support: Research supported by the National Institute on Drug Abuse of the National Institutes of Health, Award Number U10DA020024 (PI: Trivedi).

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SEX DIFFERENCES IN PATTERNS OF ALCOHOL USE AMONG NIGHTCLUB PATRONS IN BRAZIL.

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Aims: To describe sex differences in the patterns of alcohol use in the nightclubs of the city of São Paulo, Brazil by comparing entrance and exit breath alcohol concentration (BrAC), alcohol doses, type of alcoholic beverage, signs of intoxication, considering sociodemographic variables.
Methods: A representative sample of São Paulo's nightclubs in 2013 was drawn and a systematic sampling was used to recruit patrons at 31 nightclubs to answer questions from a three-step portal survey: entrance and exit interviews and an online interview 24 hours after being in a nightclub. An entrance acceptance rate of 80% generated a sample of 2422 completed interviews. The three questionnaires were answered by the same person and simultaneous ethnographic data on violence and environmental factors of the nightclub was also collected. Patrons' BrAC was tested before and after nightclub entrance by breathalyzer. Weighetd analysis were carried out stratified by gender. Poisson regression was used to examine the association between doses of alcohol consumed and sociodemographics.
Results: Among drinkers, mean entrance BrAC was higher among men than among women (men= 0.31mg/L; women= 0.26mg/L, $p<0.001$). At the exit survey no differences were found between men and women (men and women = 0.39mg/L). BrAC equivalents of binge drinking behavior (>0.38mg/L) were identified in 31% of the men and 32% of the women at exit. Vodka was the alcoholic beverage most consumed by both sexes (43%; 41%, men and women, respectively). Poisson regression showed that the number of doses of alcoholic beverages consumed at São Paulo's nightclub was statistically significantly associated with male sex, being unemployed and younger ages, but not with socioeconomic status when controlled by BrAC at entrance.
Conclusions: Considering women patterns of alcohol use in nightclubs and their higher physical vulnerability for alcohol intoxication, harm reduction initiatives should target especially women at these venues.
Financial Support: FAPESP (São Paulo State Research Foundation) grant number 2011-51658-0

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BRIEF GUIDE TO PREVENT OVERDOSE FATALITY FOR PRESCRIPTION OPIOID ABUSERS: A HARM REDUCTION INITIATIVE.

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Aims: Pharmaceutical companies are required by FDA to distribute Medication Guides to patients with each pill bottle of extended-release opioids educating them on safe use. However, a large portion of overdoses occur among abusers without prescriptions. To fill this gap, a 1-page Guide was developed targeted to opioid abusers and friends/families, which provides information to reduce risk of fatal overdose.
Methods: A draft Guide was developed with input from experts. The draft addressed key risks and effective steps to intervene in 5 areas: What are the risks? What are the signs? How do I respond to an overdose in another person? What increases the risks? Help for drug treatment. Qualitative research was conducted using multiple diverse focus groups (FG) composed of 8-15 daily non-medical opioid users. Phase I focused on version (concise versus detailed) and Phase II focused on participants' understanding and acceptance of content.
Results: Phase I testing determined a concise version was preferred over a detailed one (368 vs. 611 words) but some items from the detailed version were considered valuable e.g., list of opioids. Phase II examined a single version of revised content in 2 diverse rural FG in KY and NC. Themes highlighted by both FG included the dangers of mixing drugs and alcohol and increasing doses to get high. The groups differed on preferred order of presentation of content. The recommendation to Call 911 was identified as risky in KY, but not in NC where Good Samaritan legislation was in place. FG participants highlighted key information in the Guide that was learned including <10 breaths/minute and snoring as signs of overdose. However, there was strong adherence to myth or actions that do not work and waste time in overdose response e.g., ice or cold showers.
Conclusions: A simple guide to prevent opioid overdose and its consequences was found to be useful and was accepted by nonmedical opioid users.
Financial Support: Purdue Pharma L.P.

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WITHDRAWN

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PRE-MILITARY VICTIMIZATION AND TRAUMA AMONG A SAMPLE OF JUSTICE-INVOLVED VETERANS.

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Aims: To describe the experiences of childhood victimization and traumatic events in a sample of justice-involved veterans.
Methods: Data were taken from the SAMHSA-funded MISSION DIRECT-VET (MDV) program, a 12-month wraparound service intervention to treat co-occurring substance use and mental health disorders (COD) among justice involved veterans presenting before four courts across Massachusetts. This sample consisted of 90 veterans who completed a baseline assessment that included the Posttraumatic Diagnostic Scale (PDS), PTSD Checklist (PCL), and a variety of items from National Outcome Measures (NOMS).
Results: Regarding victimization before age 18, 36% of respondents in this sample experienced physical violence from someone they did not know and 53% from someone who was known to them. Moreover, nearly one fifth of the sample (18%) experienced sexual molestation from someone who was known to them. With regard to traumatic experiences that occurred before age 18, 54% of this sample witnessed someone seriously injured, 31% witnessed a physical or sexual assault, and nearly a quarter (24%) knew of a family member or friend who died in an accident. Additional baseline needs/risk data will be included in the presentation.
Conclusions: This analysis provides a more detailed understanding of pre-military victimization and traumatic experiences of justice-involved veterans with COD. When developing veteran-centric interventions for returning veterans, clinicians and researchers should also take pre-military experiences into consideration to better address the issues that might negatively impact legal, mental health, and substance use outcomes. These findings may hold important implications for the VA's goal of reducing the number of returning veterans involved with the criminal justice system.
Financial Support: SAMHSA/CMHS 1SM058804-01; SAMHSA/CABHI 1TI023562-01; OJP/BJA 2013-RW-BX-0003

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BORDERLINE PERSONALITY DISORDER SYMPTOMS AND HIV RISK BEHAVIORS AMONG AFRICAN-AMERICAN INCARCERATED MEN.

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Aims: In order to expand HIV epidemiology knowledge regarding the influence of psychopathology, we assessed associations between Borderline Personality Disorder (BPD) symptoms and HIV risk behaviors among incarcerated men. BPD is not typically examined by HIV epidemiologists or in males.
Methods: Data were collected during the baseline (in-prison) survey of Project DISRUPT, an ongoing cohort study of African American men being released from prison in North Carolina who were in primary committed relationships at the time of incarceration (n=159). We assessed drug use and sexual risk in the six months before incarceration and BPD symptoms using a five item scale measuring the severity of distress/problems over the past 30 days caused by behaviors such as worry that someone is planning to leave you; those scoring in the 75th percentile were considered to have elevated BPD symptoms. Associations between elevated BPD symptoms and drug and sex risk outcomes were estimated.
Results: After adjusting for age, pre-incarceration concern about being able to pay bills, and depressive symptoms, BPD symptoms were associated with multiple partnerships (OR 3.17, 95% CI: 1.33-7.58), concurrent sex partnerships (OR: 3.42, 95% CI: 1.48-7.91), drug use with sex partners (OR 5.24, 95% CI: 1.29- 21.39), having sex while high (OR 3.88, 95% CI:1.45- 10.38), crack/cocaine use (OR 4.66, 95% CI 1.62-13.45), and ecstasy use (OR 4.43, 95% CI 1.39-14.10). Associations between BPD symptoms and sex risk variables were attenuated but remained significant when controlling for crack/cocaine and ecstasy use, suggesting BPD symptoms may increase sex risk in part by contributing to drug use.
Conclusions: BPD symptomology is a strong HIV risk correlate and should be considered in future HIV prevention studies among men.
Financial Support: NIDA R01DA028766. The content does not necessarily represent the views of NIDA.

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WITHDRAWN

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THE INFLUENCE OF DOPAMINE β-HYDROXYLASE GENE POLYMORPHISM -1021C Ç T ON LEVODOPA/ CARBIDOPA TREATMENT FOR COCAINE DEPENDENCE: A PRELIMINARY STUDY.

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Aims: Targeting dopamine as a medication development strategy for cocaine dependence, while conceptually justified, has failed to produce a treatment with widespread and robust clinical efficacy. Heterogeneity in the level of dopamine activity and function might be useful for identifying a subgroup of cocaine dependent patients for which dopamine-enhancement pharmacotherapy is most effective. Here we hypothesized that response to levodopa/carbidopa treatment would be greater in patients with genetically determined low levels of the dopamine metabolizing enzyme dopamine β-hydroxylase (DβH).
Methods: Seventy-one cocaine-dependent patients participated in a 12-week randomized double-blind placebo-controlled trial of levodopa with carbidopa (800/200 mg/day) and were genotyped for the dopamine β-hydroxylase gene (DBH) polymorphism, -1021C>T (rs1611115). An exploratory analysis of 21 variants in 17 additional genes previously implicated in addiction and psychiatric disorder was conducted.
Results: Using GLMM analysis, corrected for age, gender, and population structure, levodopa treatment was associated with significantly reduced cocaine positive urines based on DBH genotype. For patients with the low DβH activity genotypes (CT/TT) who received levodopa, the odds of having a cocaine-positive urine decreased significantly over treatment compared to placebo-treated patients with the CT/TT genotype ($p = 0.004$). Subjects with the normal DβH activity genotype (CC) showed no differential response to levodopa.
Conclusions: These preliminary findings suggest that treatment of cocaine dependence by levodopa/carbidopa may be influenced by DBH genotype. However, these results need to be confirmed in a larger sample focusing on the DBH polymorphism.
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FEASIBILITY AND ACCEPTABILITY OF THE IMPLEMENTATION OF PROGRAM UNPLUGGED FOR THE PREVENTION OF DRUG USE AMONG SCHOOL ADOLESCENTS IN BRAZIL.

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Aims: To evaluate feasibility and acceptability of a curricular universal school based prevention program that have shown effectiveness when previously tested in eight European countries.
Methods: 2181 students (11 to 14 y.o.) in 8 schools in 3 Brazilian cities, received 12 lessons from "Unplugged", a curricular universal school based prevention program that has shown effectiveness when tested in 8 European countries. Through 14 focus groups, 81 subjects were interviewed (students, teachers, stakeholders, program coaches and school directors). Semi-structured interviews and focus groups were used to investigate their experiences during the 4 months of implementation of the program as well as student behavior pre and post program. Badin's content analysis was used to identify thematic axis concerning feasibility and acceptability of "Unplugged".
Results: From the stakeholders, the preventive program came to fill in a gap in the availability of more systematized actions to approach the topic of drug use in schools. Teachers acquired knowledge of techniques to help them in managing groups and in pedagogical activities. One of the highlights was the experiential training for the preventive activity and the presence of coaches in the school daily life, providing the professionals with support and security. Another highlight was the program approach more oriented towards life skills, which generated changes in the behavior of the teenagers. In the students' opinion, the strength of the Unplugged was the dynamic and participatory methodology, allowing for group interactions and opening space for meeting people they were not close with. All of the groups suggested specific changes to make the program more appropriate to the Brazilian reality.
Conclusions: Unplugged has proved to be feasible to be applied with teenagers in Brazilian schools, contributing to facing the drug use problem with a less moral and more participatory and reflective approach.
Financial Support: UNODC letter of agreement 005/2013 and 007/2013, Ministry of Health of Brazil.

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ASSESSMENT OF HUMAN ABUSE POTENTIAL OF PRELADENANT (A CENTRALLY-ACTING A_{2A} ANTAGONIST) COMPARED TO PHENTERMINE AND PLACEBO IN RECREATIONAL STIMULANT USERS.

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Aims: Preladenant (PLD) is a peripherally/centrally-acting A_{2A} receptor antagonist that was being developed for treatment of Parkinson's disease. Since centrally-acting drugs have potential for abuse, the study aim was to evaluate the abuse potential of PLD compared to placebo (PBO) and phentermine (PHEN).
Methods: This was a randomized, double-blind, balanced, placebo- and active-comparator controlled 6-way crossover study. Healthy recreational stimulant users (N=31) received single oral doses of PLD (10, 30, 100 mg), PHEN (45, 90 mg) and PBO. Eligible subjects passed a qualification session to ensure they could distinguish 60 mg PHEN from PBO. Subjective measures (VAS [0-100 scale], ARCI and Subjective Drug Value) were evaluated over 24 h postdose.
Results: Mean peak (Emax) Drug Liking VAS (primary endpoint) was significantly higher for both PHEN doses compared to PBO ($p \leq 0.007$; differences of 9.1 and 19.4 for 45 and 90 mg, respectively), thereby confirming study validity. Small but statistically significant differences between supratherapeutic doses of PLD (30 and 100 mg) and PBO were observed (6.7 and 9.7, respectively; $P<0.05$). The difference between PLD 10 mg and PBO was not significant (4.9; $P=0.14$). Drug Liking Emax values for all PLD doses were significantly lower than 90 mg ($P \leq 0.004$) but not 45 mg PHEN ($P \geq 0.201$). Results on secondary endpoints were similar, with PLD showing significant effects on some but not all endpoints compared to PBO, and effects lower than 90 mg and similar to 45 mg PHEN. The dose relationship was relatively flat for PLD compared to PHEN on most endpoints.
Conclusions: In summary, PLD produced similar effects as 45 mg PHEN on subjective Drug Liking and other measures of abuse potential, indicating an increase in stimulant-like effects. However, the effects of PLD were less than those of 90 mg PHEN and the dose relationship was comparatively flat.
Financial Support: This study was funded by Merck & Co, Inc.

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IDENTIFYING LATENT CLASSES OF ADOLESCENT DRUG TREATMENT SERVICES: AN OUTCOMES ANALYSIS.

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Aims: Among adolescents enrolled in outpatient substance use treatment we: (1) describe latent classes of treatment services youth report receiving and identify covariates associated with class membership; (2) compare substance use outcomes across latent classes.
Methods: Data are from treatment providers funded by SAMHSA's CSAT; our sample was restricted to adolescents receiving only outpatient services (N= 5,527). Using 12 items from the GAIN's Treatment Received Scale spanning domains of individual-focused, family-based, and case management services, we used latent class analysis to identify classes of treatment services youth reported receiving. Latent class regression was used to examine differences in baseline covariates across classes. We then compared several statistical methods for estimating the causal effect of class membership on a distal substance use outcome while adjusting for baseline covariates.
Results: We identified Four latent classes: (1) Low Service Utilization (12% of youth); (2) Individual-Focused Services (39%); (3) Individual- and Family-Focused Services (38%); and (4) Multiple Services (11%). Latent class regression identified significant differences across classes with regard to demographics, factors related to substance use, and justice system involvement. Comparing groups on the GAIN's Substance Problem Scale without adjusting for baseline differences indicated significant differences across groups; these differences were no longer significant when adjusting for differences in baseline covariates.
Conclusions: Differences in baseline characteristics across treatment groups may account for difference in substance use outcomes; thus, accounting for baseline differences is important when comparing non-randomized treatment groups. Our results suggest that self-selection or referral may effectively match youth with appropriate services, given their baseline need.
Financial Support: Funded by NIDA grant 1R01DA015697 and SAMHSA CSAT contract #270-07-0191.

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DEVELOPING ECOLOGICAL MOMENTARY INTERVENTION CONTENT FOR RELAPSE PREVENTION.

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Aims: Cognitive Behavioral Therapy (CBT) for relapse prevention focuses on the identification of high-risk situations to enhance informed decision-making and allow for targeted coping skills. Mobile technology enables patients to identify and document triggers as they arise, thereby increasing accuracy with in-the-moment reporting and tailored intervention. This study examines ratings of high-risk emotional, cognitive, and environmental triggers from patients enrolled in methadone maintenance treatment (MMT) for the purpose of developing content for smartphone-based EMI.
Methods: Twenty-two MMT patients completed questionnaires regarding the degree to which 59 situations would increase their desire to use. Ratings were based on a 3-point Likert scale (A lot, Somewhat, Not at all). Frequency distributions and descriptive statistics were used to determine patterns of perceived risk.
Results: Situations perceived as highest risk were "feeling depressed" and "wanting to forget worries;" average ratings were greatest for these situations, with 37% and 42% of patients endorsing these as A lot, respectively. The situation perceived as least likely to cause cravings was "I can spend time with people using without using myself;" no participants endorsed A lot and 63% identified this as Not at all. Participants generally did not perceive the risk of most potential situational triggers.
Conclusions: Patients receiving MMT appear to underestimate the impact of situational triggers on craving and potential relapse. Because MMT reduces physical cravings, patients may not see the need to anticipate triggers. The salience of wanting to reduce negative affect is high regardless of MMT, indicating that patients are more aware of being triggered by negative internal states. Smartphone tools that allow patients to track triggers as they arise may increase skills in risk assessment and cue reactivity, enabling them to understand the potential risk of being around others who may still be using. CBT-based EMI can be developed to provide individualized intervention content for maintaining long-term abstinence.
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COMPUTER VS. IN-PERSON BRIEF INTERVENTION FOR DRUG MISUSE: 12-MONTH OUTCOMES.

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Aims: This study sought to compare the effectiveness of a self-directed computerized brief intervention (CBI) to an in-person brief intervention (IBI) delivered by experienced behavioral health counselors in reducing illicit drug use risks.
Methods: This two-parallel-arm randomized clinical trial enrolled 360 primary care and dental patients with moderate-risk drug use at two community health centers in New Mexico. Participants were randomly assigned to CBI or IBI. Assessments were conducted at baseline and again at 3, 6, and 12 month follow-up, and included the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) and immunoassay hair testing with gas chromatography/mass spectrometry confirmation for marijuana, cocaine, amphetamines, and opioids. Data were analyzed using generalized linear mixed models.
Results: Global ASSIST scores decreased significantly over time for both conditions ($p < .001$), but the overall test of the condition by time interaction showed no significant differential change for IBI vs. CBI ($p=.13$). Likewise, there were no significant between-condition differences in rates of drug-positive hair tests over the 12-month study period ($p=.61$).
Conclusions: A brief intervention delivered by experienced behavioral health counselors was not superior to a computerized brief intervention for drug misuse. Computer-based interventions for drug misuse may be useful in community health centers with limited behavioral health service capacity.
Financial Support: NIDA 1R01DA026003 (R. Schwartz, PI).

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STUDIES ON MEDICATIONS FOR ADDICTION TREATMENT IN CORRECTIONAL SETTINGS.

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Aims: This poster will describe the structure, organization, and study design of The Studies on Medications for Addiction Treatment in Correctional Settings (SOMATICS) collaborative trial, a harmonized, three-site initiative funded by the National Institute on Drug Abuse (NIDA). Its objective is to investigate the under-recognized and under-addressed issue of providing medications to treat opioid-dependent detainees in order to prevent post-release relapse and negative health outcomes.
Methods: Three clinical trials with 705 opioid-dependent adult participants will be conducted at jails in New York, New Mexico, and Maryland. The first site will compare extended-release naltrexone (XR-NTX) to an enhanced treatment-as-usual without medication (ETAU), the second site will compare XR-NTX with and without patient navigation (PN) to ETAU, and the third site will compare interim methadone with and without PN to ETAU. Study measures will be harmonized across the multiple treatment arms of the three trials to analyze two primary outcomes (meeting DSM-5 opioid use disorder criteria six months post-release and urine drug testing) and multiple secondary outcomes (including HIV risk behavior, days of incarceration, days of drug use).
Results: While each trial will analyze its data separately, data will be combined across sites to compare: (1) the use of medications (XR-NTX or methadone) prior to release v. ETAU; (2) the use of medications with v. without PN; (3) XR-NTX v. ETAU; (4) interim methadone v. ETAU. Data will be analyzed using mixed effects logistic regression analysis and hypotheses will be tested using the union-intersection principle.
Conclusions: Findings will inform corrections and public health officials about effective approaches to optimal treatment approaches for opioid-dependent jail inmates prior to release.
Financial Support: Financial support provided by the National Institute on Drug Abuse at the National Institutes of Heatlh, grant number U01 DA013636-08

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PATHWAYS FROM CAREGIVER PROBLEMATIC ALCOHOL USE TO CHILD INTERNALIZING AND EXTERNALIZING BEHAVIORS IN A CHILD PROTECTIVE SERVICES SAMPLE.

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Aims: In CPS, caregiver problematic alcohol use (CPAU) is a prevalent concern associated with maltreatment and child internalizing behaviors (IB) and externalizing behaviors (EB). However, the indirect pathways from CPAU to child IB and EB are unclear.
Methods: A subsample of children that remained in the home following a CPS investigation were used from the National Survey of Child and Adolescent Well-Being II. A random half sample (n=1633) was used to build two path models in Mplus to examine direct and mediated pathways from CPAU to, separately, child IB and EB. CPAU was measured with the AUDIT. Four parallel mediators were examined: exposure to violence (Violence Exposure Scale), parental monitoring (Supervision-Child Scale), physical assault (Parent-Child Conflict Tactics Scale; CTSPC), and psychological aggression (CTSPC). IB and EB were measured with the internalizing and externalizing subscales of the Child Behavior Checklist. Control variables were child age and gender, poverty, and CPS history.
Results: Physical assault (μ=.02, σ=.01, 95% CI .003-.05) and psychological aggression (μ=.05, σ=.02, CI .02-.08) each individually mediated the relationship from CPAU to IB. In the externalizing model, significant single mediators were physical assault (μ=.04, σ=.02, CI .02-.08), psychological aggression (μ=.07, σ=.02, CI .04-.11), and exposure to violence (μ=.02, σ=.01, CI .002-.04). Comparing fit indices of single and multiple mediator models, the strongest models for both IB (RMSEA=.006, p=.99; CFI=.996) and EB (RMSEA=.006, p=.99, CFI=.998) were single mediator models through psychological aggression.
Conclusions: Results suggest psychological aggression, highly prevalent in CPS families, is a crucial target of interventions for CPAU. For families with CPAU, parenting interventions must both strengthen relationships in addition to decreasing corporal punishment in order to be effective at improving IB and EB outcomes. Future research should examine the role of comorbid caregiver conditions in the model.
Financial Support: F31DA034442; T32DA015035; Doris Duke Fellow; Fahs-Beck Scholar

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CM OF SMOKING ABSTINENCE VS. CM WITH SHAPING FOR SMOKING CESSATION AMONG TREATMENT-SEEKING PATIENTS.

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Aims: Contingency management (CM) is an efficacious intervention for reducing cigarette smoking. Previous work suggested that shaping might be used to set intermediate criteria for incentive delivery between the present behavior and total abstinence and, thus, make CM more effective. This study analyzed whether CM with shaping (CMS) improves outcomes compared with CM that reinforce abstinence for smoking cessation among treatment-seeking patients in a community setting.
Methods: A total of 47 patients were randomly assigned to one of two treatment conditions: CM (N=25) or CM with shaping (CMS) (N= 22). All participants receiving a CBT intervention implemented in group-based sessions of five or six patients. Each session took about one hour, and sessions were carried out once a week over a six-week period. CM participants earned voucher-based incentives contingent on providing biochemical evidence (a negative urine cotinine test) of smoking abstinence. CMS reinforce progressive reductions in smoking according to a percentile schedule.
Results: Of the patients who received CM, 88%, completed 6 weeks of treatment, versus 95.5% of those who received CMS ($p > .05$). At the post-treatment assessment, 92% of the patients assigned to the CM condition achieved abstinence in comparison to the 90.9% in the CMS group ($p > .05$). The number of total days of abstinence during treatment was 11.32 in the CM group, versus 11.67 in the CMS group ($p > .05$).
Conclusions: Results showed no differential effects between the two CM procedures and suggested that shaping did not improve CM's effectiveness for treatment-seeking patients in a community setting.
Financial Support: This work was supported by the Spanish Ministry of Science and Innovation (MICINN) Grant and by a Predoctoral Grant BP11-031 from the Foundation for the Promotion of Applied Scientific Research and Technology in Asturias (FICYT).

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A BRIEF BEHAVIORAL ACTIVATION TREATMENT FOR SUBSTANCE USE ASSOCIATED WITH LOWER RATES OF RECIDIVISM AT A ONE-YEAR FOLLOW-UP.

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Aims: Substance users in the criminal justice system are at risk for future incarceration, and African Americans in urban areas are even more likely to be incarcerated than their white counterparts. LETS ACT is a group behavioral activation treatment tailored for minority substance users that has demonstrated efficacy in reducing depressive symptoms and rates of substance use treatment dropout. The current study expanded past work by comparing LETS ACT to a control condition to examine the effects of the treatment on recidivism.
Methods: 90 adults (M age = 41.6 years, 92.4% African American, 63.7% Male) with elevated depressive symptoms (Mean BDI Score = 13.1, SD = 6.0) were recruited from an urban inpatient substance abuse treatment center. Participants were randomly assigned to receive either LETS ACT or supportive counseling (SC), a nondirective time-matched control treatment. Both conditions included five treatment sessions over three weeks. Participants were assessed at treatment discharge and at one-, three-, six-, and twelve-month follow-ups. Incarceration status was obtained via self-report and tracking through local and federal incarceration databases.
Results: Demographics, drug use, and depressive symptoms were equivalent at baseline across treatment conditions. Cox proportional hazards survival analysis was used to examine the association between treatment condition and total number of days until any incarceration. This discrete-time survival analysis indicated that participating in LETS ACT was associated with a lower probability of incarceration across time, B = 0.67, SE = 0.35, Wald = 3.60, hazard ratio = 1.96 (95% CI, .978-3.91), p = .05.
Conclusions: The results of this study indicate LETS ACT is associated with a nearly two-fold decrease in the likelihood of becoming incarcerated on any given day after residential treatment discharge. LETS ACT is a straightforward intervention that may be disseminated to help substance users avoid future incarceration.
Financial Support: National Institute on Drug Abuse (R01 DA026424).

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ABUSE POTENTIAL OF A DUAL OREXIN RECEPTOR ANTAGONIST: A RANDOMIZED, DOUBLE-BLIND, CROSSOVER STUDY IN RECREATIONAL DRUG USERS.

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Aims: Almorexant (ALMO) is a dual orexin receptor antagonist (DORA), a class that has shown promise for treating insomnia and substance abuse. Since hypnotics are associated with misuse, a lack of abuse liability of DORAs would offer benefits over current therapies. Therefore, the aim of this study was to evaluate the abuse potential of ALMO.
Methods: This was a randomized, double-blind, double-dummy, placebo- (PBO) and active-comparator controlled 6-way crossover study. Healthy recreational CNS depressant users (N=33 completers) received single oral doses of ALMO (200, 400, 1000 mg), zolpidem (ZOL) (20, 40 mg), and PBO. Subjects passed a qualification session to ensure they could distinguish the effects of 30 mg ZOL from PBO. In the main study, subjective measures of abuse potential (visual analog scales [VAS], Addiction Research Center Inventory, Subjective Drug Value) and objective measures (Divided Attention [DA]) were evaluated over 24 h postdose.
Results: Drug Liking VAS peak effect (Emax; primary endpoint) was significantly higher for all doses of ALMO and ZOL compared to PBO ($P<0.001$). ALMO 200 mg showed significantly less Drug Liking than both ZOL doses ($P<0.01$) and ALMO 400 mg had smaller effects than ZOL 20 mg ($P<0.05$), while ALMO 1000 mg was not different from either ZOL dose. Results were similar for other subjective measures, although ALMO generally showed smaller negative and perceptual effects compared to ZOL. ALMO also showed less cognitive impairment compared to ZOL on most DA endpoints.
Conclusions: These results showed the potential for abuse of a DORA, a class of compounds that is promising for the treatment of sleep and substance abuse disorders. Although the results suggest that individuals who abuse sedatives may "like" sedative effects, the degree of actual abuse may be different in insomnia patients or the general community.
Financial Support: This study was funded by Actelion.

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ARE SLEEP DISTURBANCES ASSOCIATED WITH CRAVING INTENSITY? WHAT IS THE INFLUENCE OF PSYCHIATRIC COMORBIDITY AND TYPE OF SUBSTANCE ON THIS RELATIONSHIP? A COMPUTERIZED AMBULATORY MONITORING STUDY IN PATIENTS BEGINNING TREATMENT FOR ADDICTION.

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Aims: Previous studies have reported sleep disturbances among patients with substance use disorders. However, few studies have explored the relationship between drug craving and sleep impairment. This study used Ecological Momentary Assessment (EMA) in patients beginning treatment for addiction, to assess the prospective association between craving and sleep disturbances.
Methods: Participants were recruited from an outpatient addiction clinic. Craving was assessed in real time with four daily assessments during their first two weeks of treatment. Sleep characteristics were assessed each morning during the same period. Data were submitted to Hierarchical Linear Model (HLM) analysis to test the effect of sleep on craving intensity. Analyses were adjusted on age, gender, psychiatric comorbidity and type of substance.
Results: 159 participants (67% males, 37 y.o.) were recruited and main substance-problem was alcohol (n=48), opiates (n=33), tobacco (n=43) and cannabis (n=35). Multi-level models indicated that insomnia symptoms during the night were associated with higher craving intensity the subsequent day (β= 0.28, T-ratio= 2.41, df = 1652, p= 0.016). After adjustment on psychiatric comorbidity, this relationship remained significant only among patients with current mood disorders. Higher craving intensity during the day was also found predictive of shorter sleep duration (< 6 h) the night after (β= 0.16, T-ratio= 2.33, df = 1632, p= 0.020), and more importantly in the tobacco group.
Conclusions: Based on these results, we hypothesize a link between sleep disturbances and craving that could be mediated by psychiatric symptoms. The nature of this link has to be further studied as craving might also influence sleep impairments.
Financial Support: PHRC 2006, MILDT 2010, CRA 2009, PRA-CNRS-CHU 2008, CNRS ATIP

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ABUSE POTENTIAL STUDY OF INTRAVENOUS OXYCODONE HYDROCHLORIDE ALONE OR IN COMBINATION WITH INTRAVENOUS NALTREXONE IN NONDEPENDENT, RECREATIONAL OPIOID USERS.

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Aims: ALO-02 is an opioid formulation intended to deter abuse; it comprises capsules filled with pellets of extended-release oxycodone hydrochloride surrounding sequestered naltrexone. The abuse potential (i.e., drug liking and high) of intravenous (IV) oxycodone combined with naltrexone, to simulate IV administration of crushed ALO-02 in solution, was compared with IV oxycodone alone and IV placebo in nondependent, recreational opioid users.
Methods: A single-center, randomized, double-blind, placebo-controlled, 3-way crossover study with naloxone challenge, drug discrimination, and treatment phases. Treatments included: IV oxycodone HCl 20 mg, IV simulated ALO-02 (20 mg oxycodone HCl/2.4 mg naltrexone), or placebo (IV 0.9% sodium chloride). The primary endpoints were drug liking and high visual analog scale. The principal parameters were peak effects (Emax), and the effects within 2 hours postdose (AUE0-2h).
Results: 33 participants (88% males, 88% white, mean age 26 years) were randomized into treatment phase and 29 completed all treatments. Study validity was confirmed with statistically significant differences in medians between oxycodone 20 mg and placebo for drug liking and high ($p<0.0001$). IV administration of simulated ALO-02 resulted in significantly lower scores than IV oxycodone on drug liking (Emax: 58.2 vs. 92.4; AUE0–2h: 104.3 vs. 152.4, respectively) and high (Emax: 17.2 vs. 93.1; AUE0–2h: 12.0 vs. 133.6), $p<0.0001$ for all comparisons. More adverse events (AEs) occurred with oxycodone (N=27, 90%) than with IV simulated ALO-02 (N=4, 12.5%) and placebo (N=2, 6.5%). The only common AE (≥5% of participants) for simulated ALO-02 was headache (N=2, 6.3%).
Conclusions: IV administration of simulated ALO-02 resulted in significantly lower abuse potential scores of drug liking and high than IV oxycodone in nondependent, recreational opioid users.
Financial Support: The study was sponsored by Pfizer Inc.

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BUPRENORPHINE/NALOXONE PEDIATRIC INGESTION: EXPOSURE RATES DIFFER BETWEEN FILM AND TABLET FORMULATIONS.

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Aims: Buprenorphine ingestion can cause life-threatening poisoning in young children. Previous reports have found that film formulations are associated with lower pediatric exposure rates than tablet formulations. The purpose of this study is to determine whether these relationships are stable over time.
Methods: Data from Researched Abuse, Diversion, and Addiction-Related Surveillance (RADARS®) System Poison Center Program, January 2011 – March 2013, involving unintentional exposure to buprenorphine sublingual tablets or film by children aged < 6 years were analyzed. To adjust for medication availability, event ratios (rates) were based on the number of patients filling prescriptions for each formulation ("Unique Recipients of a Dispensed Drug", URDD). Negative binomial regression was used to produce quarterly rates, average rates, and 95% confidence intervals (CIs).
Results: 1,695 reports were analyzed. Exposure rates for buprenorphine/naloxone combination tablets (7.0 exposures per 10,000 URDD (CI: 6.6 – 7.3)) exceeded those for buprenorphine monoingredient tablets (2.8 (CI: 2.4 – 3.2)) and combination film (0.9 (CI: 0.8 – 1.0)). The combination tablet and monoingredient tablet rates were significantly greater than film rates (Rate Ratios (RR): 7.6 (CI: 6.7 – 8.6; $p<0.0001$) for combination tablets and RR: 3.1 (CI: 2.6 – 3.7; $p<0.0001$) for monoingredient tablets compared with film, $p<0.0001$ for each). Relationships were consistent over time except for slight decreases in the monoingredient tablet rate.
Conclusions: The rate of unintentional exposures to buprenorphine/naloxone sublingual film by young children is significantly less than the rate of exposure to buprenorphine/naloxone or buprenorphine monoingredient tablets.This study cannot determine whether the differences are caused by packaging or formulation.
Financial Support: Reckitt-Benckiser Pharmaceuticals

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REGIONAL CONCENTRATIONS OF OPANA® ER ABUSE BEFORE AND AFTER INTRODUCTION OF A TAMPER-RESISTANT FORMULATION IN 2012.

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Aims: Abuse of Opana® ER (extended release (ER) oxymorphone tablet) significantly increased following the reformulation of OxyContin® (ER oxycodone) and declined following introduction of the tamper resistant Opana ER in February 2012. We examined regional differences in abuse of Opana ER before and after the introduction of the reformulation within the United States.
Methods: Researched Abuse, Diversion, and Addiction Related (RADARS®) System Poison Centers recorded abuse exposures to Opana ER one year before and after introduction of the reformulation (2011Q1 - 2011Q4 and 2012Q3 - 2013Q2). Zero-inflated Poisson regression was used to assess changes in cases and rates across poison centers. Rates represent mentions over prescriptions filled within ZIP codes served by the regional poison center.
Results: Opana ER abuse exposures declined from 255 in the year before introduction of the reformulation to 73 in the year after reformulation, a 74% (95% CI: 61% to 83%, $p<0.001$) decline. The number of exposures reporting injection use of Opana ER were 17 before and 25 ($p=0.081$) following the reformulation. Declines were also observed adjusting for prescriptions dispensed. Five of 43 poison centers accounted for 57% of pre-reformulation abuse exposures: Kentucky, Upstate New York, California, West Virginia, and Tennessee. Following the reformulation, the number of Opana ER exposures reported to these centers declined except for Tennessee. Tennessee accounted for 21% of post-reformulation cases and 32% of exposures reporting injection use.
Conclusions: Abuse of Opana ER reported to poison centers declined following the reformulation. In both time periods, exposures and route of administration appear to be concentrated in specific regions of the United States.
Financial Support: The RADARS® System is part of Denver Health and Hospital Authority, a division of the state of Colorado. It is supported by subscriptions from pharmaceutical manufacturers.

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MARIJUANA USE AND ITS RELATIONSHIP TO IMPULSIVITY MEASURED VIA DELAY DISCOUNTING.

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Aims: The use of illicit drugs has been identified as one of the six leading health-risk behaviors contributing to death and disability among youth. Prior research suggests that substance users tend to rate higher on measures of impulsivity than non-users. However, most research has focused primarily on distinguishing between users and non-users, while not assessing for whether the user has only tried the substance in the past. The present study aimed to examine the relationship between impulsivity and marijuana use status in a sample of adolescents and emerging adults.
Methods: We used Analysis of Variance (ANOVA) to examine data gathered from adolescent and emerging adult participants concerning their scores on a behavioral measure of delay discounting (a facet of impulsivity) and marijuana use. Marijuana use status was coded using three conditions: never used marijuana (n = 55), tried it in the past (n = 26), and currently use it (n = 18).
Results: Our one-way ANOVA analysis revealed a significant effect of marijuana use status on levels of impulsivity for the three conditions [F (2, 96) = .937, p < .05]. Our results indicated that current users of marijuana were rated as the most impulsive (M = -.35, STD = .46), followed next by those who have tried marijuana in the past (M = -.14, STD = .51). Those who reported never having used marijuana were rated as the least impulsive (M = .01; STD = .56). Interestingly, this same analysis was repeated using cigarette smoking status (divided into current smokers, triers, and nonsmokers) and the results were non-significant.
Conclusions: These findings add novel data to the literature on status of illicit substance use and impulsivity, highlighting the importance for future researchers to not only assess for current substance use, but also for whether the individual has tried said substance in the past. These findings could potentially inform future intervention programs targeting illicit substance use in adolescents and emerging adults, a population that is particularly vulnerable to risky health behaviors and their negative life consequences.
Financial Support: TAMU Vision 2020 Dissertation Enhancement Award

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EVALUATION OF INTRAVENOUS SELF-ADMINISTRATION OF ALKS 33 IN RATS TRAINED TO SELF-ADMINISTER MORPHINE.

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Aims: The reinforcing properties of ALKS 33 were evaluated relative to morphine.
Methods: Male S-D rats (N=15) trained to lever press for food under a FR5 response schedule were surgically prepared with an indwelling femoral catheter and 0.56 mg/kg/inj morphine was made available for IV self-administration (SA) during 1-hr training sessions. Three additional doses of 0.1, 0.3 and 1.0 mg/kg/inj were also evaluated to characterize morphine. Potential reinforcing properties of ALKS 33 were then evaluated by substituting vehicle, escalating doses of ALKS 33 (0.0136, 0.0408 or 0.068 mg/kg/inj), or the morphine training dose for SA in a within-subject design. Morphine SA was considered stable when the number of infusions was within 30% variability at least 3 of 5 test days.
Results: The mean number of infusions self-administered at all doses of ALKS 33 was significantly lower than the mean number of morphine infusions. However, despite a much smaller effect size, mean infusions of ALKS 33 were also significantly higher than the mean number of self-administered saline infusions. Important to note is that mean saline infusions were low due to the protocol-driven criteria for extinction. Because of this observation, additional post-hoc analyses were performed. Time required for rats to pass vehicle extinction criteria after morphine SA was nearly three times longer than that required to pass vehicle extinction after ALKS 33 SA (~14 vs. ~5 days, respectively). Furthermore, the mean number of saline infusions 5 days following morphine SA was approximately three times higher than the mean number of saline infusions 5 days following ALKS 33 SA.
Conclusions: These findings indicate that IV SA of ALKS 33 did not function as a reinforcer similar to morphine. Finally, this SA analysis approach provides an additional method for examining and understanding complex data generated using this standard paradigm.
Financial Support: This study was funded by Alkermes, Inc.

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PERCEIVED DRINKING RISK AND ADOLESCENT ALCOHOL USE OVER TIME: A DUAL LATENT GROWTH CURVE ANALYSIS.

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Aims: Early initiation of alcohol use is associated with increased risk for later alcohol use disorders. The need to predict and prevent underage drinking is a top public health priority targeted by the Surgeon General. Lower perceived drinking risk and more positive alcohol expectancies predict greater alcohol use, but less is known about how early perceived drinking risk influences change in drinking over time. We hypothesized that youth with more positive and fewer negative alcohol expectancies and who perceived alcohol to be less risky would increase more quickly in their drinking over time.
Methods: 246 children participated in a longitudinal study on risk behaviors (56% male; mean age=13, SD=.90; 48% White, 36% Black, 16% other). Adolescents reported drinking frequency and perceived drinking risk annually for 4 years using a version of the Youth Risk Behavior Surveillance System. We tested a model in which baseline levels of perceived drinking risk, actual alcohol use, and alcohol expectancies predicted rate of change in perceived risk and alcohol use over time.
Results: We specified dual latent growth curves capturing change in perceived drinking risk and actual alcohol use. The model fit the data well (RMSEA=0.04). Perceived drinking risk significantly decreased over time, whereas drinking behavior significantly increased. Higher perceived drinking risk at baseline predicted a slower increase in drinking over time (B=-0.28, p=.065). More positive alcohol expectancies predicted a steeper decline in perceived drinking risk (B=0.07, p=.005), whereas more negative expectancies predicted a less steep decline in perceived drinking risk overtime (B=-0.08, p=.01).
Conclusions: Greater perceived drinking risk and more negative expectancies serve a protective function whereby adolescents increase their alcohol use more slowly over time. These findings can inform prevention efforts focused on decreasing alcohol initiation and use. Results are discussed within a developmental psychopathology framework that considers both risk and protective mechanisms related to alcohol involvement.
Financial Support: NIDA R01 DA018647-09

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USE OF REAL-TIME FUNCTIONAL MAGNETIC RESONANCE IMAGING FOR FACILITATION OF SELF-REGULATION OF NUCLEUS ACCUMBENS RESPONSE IN COCAINE ABUSERS.

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Aims: Chronic cocaine abusers show enhanced sensitivity to cues for cocaine within the nucleus accumbens (NAc), of magnitude correlated with subjective craving levels. Modulation of this enhanced NAc response may thus hold significant therapeutic value. Technologies including TMS/TDCS afford externally-mediated modulation of neural responses; however, research indicates that modulation of neural activity can also be initiated through internally-promoted self-regulatory processes. The present study used real-time fMRI neurofeedback to facilitate the self-regulated modulation of NAc responses to cocaine cues in chronic cocaine abusers.
Methods: Sixty-two participants meeting criteria for past cocaine abuse performed a cue-elicited craving task while real-time fMRI neurofeedback indicated the current state of bilateral NAc response via an on-screen thermometer. On separate trials, participants were instructed to either MAINTAIN or DECREASE the height of the thermometer, while viewing pictures of cocaine, food, or neutral stimuli. In two control conditions, real-time neurofeedback was linked to the anterior cingulate (ACC) or the auditory cortex (AuC).
Results: Forty-two participants (defined as "responders") showed increased NAc response to cocaine cues compared to neutral cues, indicating baseline reponsivity to cocaine cues. Comparison of CocaineWATCH trials to CocaineDECREASE trials indicated that these responders showed successful NAc downregulation in the CocaineDECREASE condition. This NAc downregulation was not seen when the neurofeedback was linked to activity in the ACC or AuC.
Conclusions: The use of real-time fMRI-based neurofeedback may facilitate cocaine abusers self-regulation of altered NAc activity to cocaine cues. Future work should evaluate the longevity of this modified neural response, and its relationship to subjective craving levels.
Financial Support: NIDA: 5R21DA077149 and 1R21DA029464, awarded to M. Shane

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CEASE QUIT SMOKING; A SUCCESSFUL CBPR TRIAL.

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Aims: Smoking disproportionally affects underserved populations but only a handful of interventions have demonstrated to be effective when taken into real-life situations. We used a Community-Based Participatory Research approach to test an intervention with experimental methodology.
Methods: A total of 352 participants were randomized to either of two group-based interventions. Treatment effects were evaluated through self-report smoking abstinence and verified by expired-air carbon monoxide. Both interventions included 12 tobacco cessation sessions with health education, motivational exercises, and NRT. They were implemented at churches and schools by Peer Motivators, with varying contingency behavioral management programs for session attendance and landmark achievements (Group "A" had monetary rewards only and Group "B" combined monetary and non-monetary rewards). A total of 352 participants were recruited (58% men; 65% African Americans; 82% were 40 years or older, 78% did not have a job). About 53% of participants completed a final questionnaire.
Results: Intent to treat analyses revealed that 27% of participants in Group "A" and 29% in Group "B" were able to quit smoking (Pr=0.675). Multivariate analyses showed that session attendance was strongly associated with quitting smoking (RR=1.2 per session; 95% CI = 1.1.-1.4, p <0.001), those with less than a high school (RR=2.1 per session, 95% CI = 1.0.-4.0, p<0.05); and those with higher health problems (RR=1.2 per reported problem, 95%CI = 1.0-1.4, p <0.05). Those who attended 50% or more sessions had better success rate (40.0%) vs. those who attended between 20 and 50% of the sessions (31.9%), and vs. those who have <20% attendance (6.4%).
Conclusions: Community engagement in the design, implementation and evaluation of a smoking cessation program involving Community Peer Motivators can be successful among low income populations.
Financial Support: Supported by grant R24 MD002803 from the National Institute of Minority Health and Health Disparities.

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WITHDRAWN

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INVOLVEMENT OF MGLU5 RECEPTOR SIGNAL CASCADE IN THE ENHANCEMENT OF MORPHINE-INDUCED HYPERLOCOMOTION UNDER CHRONIC TREATMENT WITH ZOLPIDEM.

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Aims: Zolpidem, a GABAA receptor α1 subunit agonist, is the most widely prescribed hypnotic drug and it has been reported that zolpidem induces physical and psychological dependence. Even though, drug dependence is considered to be related to the neuro plastical changes in the mesolombic system, underlying mechanisms of drug dependence induced by zolpidem is not fully understood. On the other hand, it is well known that the balance between the GABAergic and glutamatergic systems plays a critical role in maintaining the neuronal network. Furthermore, metabotropic glutamate receptors (mGluR) interact with GABAergic signaling. Therfore, the present study was designed to investigate the interaction between GABA receptor and mGlu5 receptor in the limbic forebrain including the N.Acc. after treatment with zolpidem. In addition, we also examined the influence of zolpidem on the mGlu5 receptor cascade and on dopamine-related behavior.
Methods: The locomotor activity of mice was measured by tilting-type cage. Total activity counts were automatically recorded for 3 hr after morphine treatment. Brain tissue was prepared for biochemical assays after treatment with zolpidem for 7 days.
Results: mGlu5 receptor protein levels were significantly increased by treatment with zolpidem (30 mg/kg, s.c.) for 7 days in the limbic forebrain. To confirm that mGlu5 receptor is directly involved in dopamine-related behavior in mice following chronic treatment with zolpidem, we measured morphine (10 mg/kg, i.p.)-induced hyperlocomotion after chronic treatment with zolpidem in the presence or absence of an mGlu5 receptor antagonist MPEP (100 nmol/mice i.c.v.). Although chronic treatment with zolpidem significantly enhanced morphine-induced hyperlocomotion, this enhancement of morphine-induced hyperlocomotion was suppressed by treatment with the MPEP.
Conclusions: These results suggest that chronic treatment with zolpidem caused activation of the mesolimbic dopaminergic system accompanied by an increase in mGlu5 receptor.
Financial Support: Grant support: 25430076

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CHILDHOOD MALTREATMENT AND ADOLESCENT BINGE DRINKING: NEW FINDINGS ON A LONGITUDINAL RELATIONSHIP.

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Aims: Exposure to childhood maltreatment (CM) has been linked to adolescent binge drinking (BD) in numerous cross-sectional studies. However, few studies explored the longitudinal relationship between CM and adolescent BD. Given the developmental nature of adolescent BD, we examined the effects of CM on the longitudinal course of adolescent and young adult BD, as CM might be a significant factor in predicting continuing BD beyond adolescence.
Methods: Longitudinal data were drawn from the National Longitudinal Study of Adolescent Health (AddHealth), which is a longitudinal study of adolescents (grades 7–12) in the U.S., exploring the influence of social environment on health in adolescence. Using the nationally representative sample of adolescents (N=8,503), we performed two separate growth curve modeling analyses to examine the effects of subtype (e.g., physical, sexual abuse, neglect) and frequency of CM on BD trajectories from adolescence to young adulthood (ages 12-32). We controlled for common risk factors for adolescent BD such as parental alcoholism, peer BD, and adolescent depression in all analyses.
Results: We found that compared to respondents who never experienced any CM, respondents with a history of childhood neglect and/or physical abuse experienced a steeper increase in rates of BD (β = 0.07 – 0.08) during adolescence and persistently higher BD (β = – 0.01) beyond adolescence and throughout much of young adulthood. The frequency model indicated that greater frequency of neglect and physical abuse, either alone or in conjunction, was also associated with steeper increases in BD rates (β = 0.02 – 0.03) during adolescence and persistently elevated BD (β = – 0.01) over time.
Conclusions: The present study suggests that child neglect and physical abuse might have long-lasting adverse effects on BD beyond adolescence and throughout much of young adulthood. Our results also suggest the need for prevention and intervention efforts implemented throughout adolescence and young adulthood for those individuals who suffered childhood neglect and physical abuse.
Financial Support: Partially supported by the Silberman Grant Fund to Sunny Shin (PI)

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PREDICTORS OF CHANGES IN SMOKING FROM 3RD TRIMESTER TO 9 MONTHS POSTPARTUM.

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Aims: Although about 45% of women stop or reduce smoking during pregnancy, over half relapse to smoking after child birth. Though it is clear that there are individual differences in trajectories of smoking postpartum, the goal of this study was to identify predictors of these individual differences in relapse trajectories.
Methods: Smoking (n = 163) and demographically similar non-smoking (n = 80) pregnant women were recruited prenatally. Maternal smoking was assessed through a combination of self-report, cotinine in saliva, and infant meconium at delivery. We used multilevel models to analyze changes in average number of cigarettes per day across four time points (preconception, 3rd trimester, 2 and 9 months postpartum).
Results: On average, women nearly returned to their levels of preconception smoking (M = 7.69, sd = 8.33) by 9 months postpartum (M = 4.58, sd= 5.25). Time accounted for 55% of individual differences in smoking. Though the model included maternal anger, race, marijuana and alcohol use as well as child's gestational age, the only significant predictor of changes in smoking postpartum was partner smoking status. Relative to women with no partner, women with non-smoking partners had lower rates of change in smoking (β=-0.59, SE=.28, p=.035), but having a smoking partner was virtually the same as having no partner (β=0.09, SE=.38, p=.816). Average marijuana use predicted smoking at the 3rd trimester (β=0.59, SE=.21, p=.006), but did not predict change in smoking from 3rd trimester to 9 months postpartum.
Conclusions: Our results suggest that timing of relapse prevention interventions for pregnant and postpartum smokers is crucial. With women nearly returning to preconception smoking levels by 9 months postpartum, interventions should be targeted early in the postnatal period. In addition, having a non-smoking partner seems to be a protective factor against increases in smoking postpartum, so interventions should include partners to maximize effectiveness.
Financial Support: R01DA019632 (RDE).

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NICOTINE CONSUMPTION AND DEPENDENCE: GENETIC AND ENVIRONMENTAL RISK FACTORS SHOW INDIRECT EFFECTS THROUGH NICOTINE CRAVING.

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Aims: *CHRNA5/A3/B4* gene variation, adverse childhood events, and parental history of smoking problems are established risk factors for nicotine phenotypes, e.g., cigarettes per day (CPD) and the Fagerstrom Test for Nicotine Dependence (FTND), but less is known about mechanisms for these associations. Craving is considered a proximal cause of smoking that plays a key role in nicotine disorders. We examined if craving mediates the relationships between these risk factors and nicotine phenotypes.
Methods: From an Israeli adult household sample, 658 lifetime smokers were evaluated with a structured interview. Regression and bootstrapping procedures assessed the total and direct effects of the three risk factors on CPD and FTND and their indirect (mediated) effects through craving.
Results: All risk factors had significant total effects on CPD and FTND and indirect effects through craving. For example, *CHRNA5/A3/B4* (presence of allele G at variant rs3743078) indirectly increased CPD by 3.5 cigarettes (95%CI=1.2,5.7) due to the association between *CHRNA5/A3/B4* and craving. Similar indirect effects were seen for childhood adversity (2.8 cigarettes; 95%CI=1.4,4.4) and parental history (1.7 cigarettes; 95%CI=0.6,3.0). For FTND, *CHRNA5/A3/B4* was associated with a 0.4 point increase in FTND score (95%CI=0.3,1.2) due to the association between *CHRNA5/A3/B4* and craving. Similar indirect effects were seen for childhood adversity (FTND increase 0.6; 95%CI=0.3,0.9) and parental history (FTND increase 0.4; 95%CI=0.1,0.6). The association of each risk factor with craving explained a sizeable portion of that risk factor's total effect on CPD (48.0%-79.0%) and FTND (56.5%-80.6%).
Conclusions: The association of *CHRNA5/A3/B4*, childhood adversity, and parental nicotine problems with nicotine consumption or dependence is partially explained by the association of these factors with nicotine craving. This study provides important insight into nicotine related behaviors and support nicotine craving as a therapeutic target.
Financial Support: R01AA013654, R01DA018652, K05AA014223, T32DA031099, New York State Psychiatric Institute

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PHARMACOKINETIC-PHARMACODYNAMIC ANALYSES IN THE ASSESSMENT OF ABUSE-DETERRENT OPIOID FORMULATIONS.

Megan Shram[1], Salvatore Colucci[2], Stephen Harris[2], Peter J Perrino[2], Kerri A Schoedel[1], Naama Levy-Cooperman[1], Sharon L Walsh[3]; [1]Altreos Research Partners Inc., Toronto, ON, Canada, [2]Purdue Pharma LP, Stamford, CT, [3]Department Behavioral Science, University of Kentucky, Lexington, KY

Aims: ADFs are being developed to mitigate opioid abuse while maintaining patient access to safe and effective analgesic therapy. It is generally expected that reducing and delaying peak opioid agonist concentration (Cmax) reduces abuse potential. To evaluate the utility of PK in assessing abuse deterrence, this exploratory analysis focused on the relationship between PK and subjective PD measures (eg, bipolar Drug Liking visual analog scale) commonly used in human abuse potential (HAP) studies.
Methods: Pearson correlations were conducted using time-matched data and derived parameters (eg, Cmax and peak effect [Emax]) obtained following administration of both ADF and non-ADF formulations via different routes of administration (ROA).
Results: The PK/PD relationship is dependent on ROA and PK profile variability. Time to Drug Liking Emax varied systematically with speed of opioid delivery and ROA (eg, 18, 50 & 78 min after intravenous, intranasal and oral administration of ~doses of oxycodone). Correlations between time-matched PK/PD data, and between Cmax/Emax, were generally weak (r<0.25). However, when formulations were manipulated using different tampering methods that resulted in more variable exposure, stronger overall Cmax/Emax correlations were observed (r>0.45). The PK/PD relationship was more complex for agonist/antagonist combination ADF than for physicochemical barrier ADFs for there was no relationship between antagonist exposure and subjective response (r<0.1). The relationship between opioid exposure and pupillary miosis was more robust (time-matched or derived parameters; r>0.4).
Conclusions: The PK/PD relationship for abuse potential is highly variable and is influenced by numerous factors, including dosage form manipulation and ROA. Effects unrelated to opioid exposure impact a subject's drug experience. PK alone cannot be used to reliably assess abuse deterrence in HAP studies.
Financial Support: Supported by Altreos Research Partners, Inc. and Purdue Pharma LP.

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DEVELOPING AN EVIDENCE-BASED INTERVENTION TARGETING HIGH-RISK MIGRANT WORKERS.

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Aims: Nepal has a concentrated HIV epidemic and labor migrants share the highest burden. The epidemic among migrant workers has been associated with risky sexual behaviors, and with alcohol and drug abuse. The very few HIV prevention efforts that have been attempted with this group have been unsuccessful primarily due to stigma, discrimination, and insufficient availability of culturally relevant evidence-based interventions (EBIs). In order to address this issue, we propose formative research designed to promote the development of an intervention to reduce HIV transmission risk among migrant workers in Nepal.
Methods: As we will describe in the presentation of our intervention development process, we will use the ADAPT-ITT approach for intervention adaptation – which will involve focus groups with the members of the target population and treatment providers – we will refine and adapt the Holistic Health Recovery Program (HHRP) – an evidence-based HIV risk reduction behavioral intervention – to HHRP-N(epal) for optimal use with the high-risk migrant population in Nepal. Interview items will focus on the HIV risk profile of the target population and ways to optimize the intervention content (i.e., specific content areas of the original evidence-based HHRP modules to include/exclude, emphasize/abbreviate), delivery modality (group vs. individual), and duration (length/timing). In order to develop a culturally sensitive intervention, the program will draw upon Wiley's framework that includes accommodation, incorporation, and adaptation. Together, all of these data will inform intervention adaptation and subsequent pilot testing of the adapted intervention.
Conclusions: We expect that the formative process described in this presentation will provide the empirical foundation necessary to strongly inform a subsequent extramurally funded study of an adapted EBI targeting high-risk migrant workers in Nepal.
Financial Support: None

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EXAMINING THE ASSOCIATION BETWEEN METHADONE MAINTENANCE TREATMENT AND BODY MASS INDEX.

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Aims: To examine whether changes in BMI occurred as a function of MM treatment initiation, as well as to identify potential variables that may influence changes in BMI during treatment.
Methods: A retrospective chart review was conducted for 95 outpatients who were enrolled in a MM program for >1 year and provided height and weight measurements on intake and at a subsequent assessment. Variables included height, weight, gender, methadone dose, age, intravenous or no intravenous use, primary opioid of abuse, Beck Depression Inventory, Beck Anxiety Inventory, Michigan Alcohol Screening Test and Addiction Severity Index composite scores.
Results: Participants were 38 (24-64) yrs old, 36% female and were maintained on an average methadone dose of 116 (30-260) mg. The average interval between the initial BMI assessment at intake and the second measurement was 1.8 years. BMIs significantly increased during treatment from 27.2 to 30.1, for an average BMI change of 2.9 (CI 2.2 to 3.7, 95% confidence). Gender was the strongest predictor ($p = 0.003$), with females showing significantly greater increase in BMI than males (+5.2 vs. +1.7, respectively; $p < 0.001$). No other demographic or drug use variables significantly predicted BMI change during treatment.
Conclusions: Data from this retrospective chart review suggest that enrollment in MM treatment may be accompanied by an increase in BMI, particularly among female patients. While future studies should more rigorously investigate weight change during opioid maintenance, as well as the underlying mechanisms, these data highlight the likely importance of weight monitoring and provision of nutrition-related education and support to help patients mitigate potential weight gain during treatment.
Financial Support: This research was supported in part by NIH COBRE award P20GM103644 from the National Institute of General Medical Sciences.

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SEXUALLY DIMORPHIC EFFECTS OF EARLY LIFE EXPERIENCE AND ADOLESCENT Δ-9-TETRAHYDROCANNABINOL EXPOSURE IN THE RAT.

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Aims: This study aims to examine behavioral differences in male and female rats either shipped at postnatal day 14 (P14) or vivarium reared following exposure to Δ-9-tetrahydrocannabinol (THC) during adolescence.
Methods: Animals either arrive as intact litters of 5M and 5F with the dam at P14 or are born in our vivarium and subjected to our standard rearing/handling protocol (weekly weighing starting at P1). At P21 all animals are weaned and housed 2-3/cage in same sex same treatment groups. Dosing with 3mg/kg THC occurs once daily P29-P38. One group of animals is tested on the elevated plus maze (EPM) and forced swim test (FST) on P39 and P40, respectively. Another group is tested in the pre-pulse inhibition (PPI) task on P48.
Results: Preliminary results (n=5-6/group) indicate that vehicle treated shipped males exhibit a depressive-like phenotype in the FST and that adolescent THC exposure reverses this. Additionally, shipped THC males spend more time on the open arms of the EPM, indicating less anxiety compared to control shipped males.
In comparison to males, females overall spend more time in the open arms of the EPM and have an increased latency to immobility in the FST (an antidepressant phenotype), but show no significant changes in these behaviors due to either shipping or THC treatment.
In PPI, both males and females showed a dampening of the PPI response (a pro-psychotic response) with THC treatment only if they were born in the vivarium, and the effect was greater in males than in females.
Conclusions: Male and female rats differ in their behavioral reactions to both shipping and adolescent THC exposure. Males appear to be more affected by shipping during early life and this experience also seems to increase their sensitivity to adolescent THC treatment with respect to measures of anxiety and depression. Conversely, animals of both sexes without shipping in early life appear to be more susceptible to psychotic-like symptoms due to adolescent THC exposure, with this effect being more robust in males than females.
Financial Support: NIH P50 DA 025484-0001

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SELF-EFFICACY MEDIATES TREATMENT OUTCOME IN A SMOKING CESSATION PROGRAM FOR ADOLESCENT SMOKERS.

Patricia Simon, Christian Connell, Grace Kong, Meghan E Morean, Dana A Cavallo, Deepa Camenga, Suchitra Krishnan-Sarin; Department of Psychiatry, Yale School of Medicine, New Haven, CT

Aims: Research supports the efficacy of cognitive behavioral therapy (CBT), abstinence-contingent incentives (CM) and CM combined with CBT (CM+CBT) for smoking cessation among adolescents. The mechanisms of adolescent smoking cessation interventions, however, are unclear. Therefore, the purpose of this study was to examine the mechanisms through which these interventions affect smoking cessation. Specifically, we examined whether self-efficacy to resist smoking mediated the effect of CM, CBT and CM + CBT on smoking cessation.
Methods: Participants were 82 predominantly White (93%) adolescent smokers (54% female) randomized to one of three 4-week interventions: CM (n = 25), CBT (n = 26) or CM + CBT (n =31). At baseline and at the end of treatment, adolescents reported on their self-efficacy to resist smoking when emotionally stressed. The primary outcome for smoking was self-reported number of days of cigarette use during the last 7 days of treatment.
Results: Using regression analyses, we controlled for baseline levels of self-efficacy and found that self-efficacy to resist smoking when emotionally stressed (assessed at the end of treatment) mediated the effect of CM + CBT on number of days of cigarette use over the last week of treatment (indirect effect = -.24, p= .02, 95% CI = -.29 to -.05). In particular, relative to participants in the CBT condition, participants in the CM + CBT condition experienced higher levels of self-efficacy to resist smoking while emotionally stressed (B = .34, p = .01) which, in turn, was associated with fewer number of days smoking during the last week of treatment (B = -.75, p < .001). We did not observe a significant mediation effect when we compared CM to CBT.
Conclusions: Adolescents who participated in CM + CBT had greater self-efficacy to resist smoking when emotionally stressed relative to those who participated in CBT. CM, by helping adolescents achieve abstinence early in treatment, may enhance their ability to focus on learning and applying CBT skills.
Financial Support: This study was supported by NIDA grants # P50 DA09421 and T32 DA019426.

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IMPACT OF MARIJUANA USE ON MEMORY IN PATIENTS WITH HIV/AIDS: A SYSTEMATIC REVIEW.

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Aims: The most robust neurocognitive effect of cannabis use is memory impairment. Memory deficits are also high among persons living with HIV/AIDS, and cannabis is the most commonly used drug in this population. Yet research examining neurocognitive outcomes resulting from co-occurring cannabis and HIV is virtually non-existent. Thus, the primary objectives of this systematic review are to: (1) examine the literature specific to memory functioning in HIV-infected individuals; (2) examine the literature specific to memory functioning in cannabis users; (3) synthesize findings to propose a theoretical model; and (4) discuss directions for future research.
Methods: PubMed was searched for English publications since 2000 based on a systematic review methodology.
Results: Twenty-one studies met inclusion criteria in the HIV literature, and twenty-three studies in the cannabis literature. Among HIV-infected individuals, memory deficits with medium to large effect sizes were observed. Cannabis users also demonstrated memory impairment, but results were less consistent due to diversity of samples. Neuroimaging studies reported HIV- and cannabis-related disruptions in neural activation during memory encoding even when behavioral performance was not compromised.
Conclusions: A compensatory model, based on the cognitive aging literature, is proposed to explain the interaction between cannabis and HIV. Among healthy individuals, cannabis-related disruptions in memory processing may not be associated with memory decline. However, HIV-infected individuals likely must recruit additional brain regions during memory encoding to compensate for HIV-related decline, and the added neural strain caused by co-occurring cannabis is likely to exhaust neural resources, resulting in more significant memory impairment.
Financial Support: K23 DA-028660; F31 DA-035131

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WITHDRAWN

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A PILOT SPECIALTY JAIL DIVERSION PROGRAM FOR JUSTICE-INVOLVED VETERANS WITH CO-OCCURRING DISORDERS.

David Smelson[1,2], D A Pinals[3,2], Leon Sawh[1,2,4], C Fulwiler[2], S Singer[2], K O'Connor[2], W Fisher[4], S Hartwell[5], Gerardo Gonzalez[2]; [1]Department of Veterans Affairs, Bedford, MA, [2]University of Massachusetts Medical School, Worcester, MA, [3]Massachusetts Department of Mental Health, Boston, MA, [4]University of Massachusetts Lowell, Lowell, MA, [5]University of Massachusetts Boston, Boston, MA

Aims: To describe MISSION DIRECT-VET (MDV), a jail diversion program for justice-involved veterans with co-occurring mental health and substance use disorders (COD) and present the baseline service needs of program participants.
Methods: MDV is a 12-month wraparound intervention delivered by case manager and peer support specialist teams in four Massachusetts courts. This pilot enrolled 90 veterans who completed baseline assessments which included the ASI-Lite, BASIS 24, PCL-C, and NOMS.
Results: The sample was predominantly male (96%), Caucasian (87%) and completed some college (50%). The average age was 40, over half served in Iraq/Afghanistan (58%), most were in the Army or Marines (83%), nearly half were less than honorably discharged from the military (48%). and had an average of four prior incarcerations. Participants reported use of alcohol (52%), marijuana (18%), or cocaine (12.2%) in the 30 days before their most recent arrest while 54% of the sample reported little or no difficulty managing their daily tasks and 48% reported little or no difficulty coping with problems in the two weeks prior to baseline. Many of the participants reported a history of inpatient substance abuse (61%) and/or mental health treatment (44%) prior to entering MDV. Additional baseline needs/risk data will be included in the presentation.
Conclusions: MDV is one of the first veteran-centric programs in Massachusetts designed to divert veterans from jail into treatment. These findings have the potential to guide development of other diversion programs to meet the needs of justice-involved veterans including future Veterans Treatment Courts. An evaluation of the MDV program is underway and MISSION-Criminal Justice Treatment Manuals have been developed to assist with model fidelity and replication.
Financial Support: SAMHSA/CMHS 1SM058804-01; SAMHSA/CABHI 1TI023562-01; OJP/BJA 2013-RW-BX-0003

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ACUTE COCAINE AND CONCORDANCE ACROSS MEASURES OF IMPULSIVE CHOICE FOR FOOD.

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Aims: Several rat studies have demonstrated that chronic cocaine increases impulsive choice for food pellets (i.e., preference for a smaller, immediate food reinforcer over a larger, later one). These studies employed one of several impulsive choice procedures that can quickly assess impulsivity within one session (i.e., Fixed and Adjusting Delay procedures). However, research has yet to determine if acute cocaine produces similar effects within these procedures.
Methods: Impulsive choice was assessed twice daily in an AM (Fixed Delay) and PM (Adjusting Delay) session. Change in impulsive choice for food pellets was examined following injection of a range of acute ip cocaine doses (2, 5, & 15 mg/kg) prior to experimental sessions. Test sessions for each dose were conducted across two days in a counterbalanced fashion for the two choice procedures.
Results: Baseline levels of impulsivity were positively correlated between the two procedures. Cocaine dose dependently increased impulsivity in the Fixed Delay procedure, but had no systematic effect on impulsivity in the Adjusting Delay procedure.
Conclusions: These results were intriguing given that baseline measures of impulsivity were positively correlated between the two procedures. Possible reasons for the inconsistent effects of acute cocaine across these procedures will be discussed, including potential limitations in employing the Adjusting Delay procedure to measure drug effects.
Financial Support: Research was supported by NIH grants P50 DA033942-02 (MEC) and T32-DA007097-32

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THE IMPACT OF CANNABIS USE ON OPIOID-DEPENDENCE TREATMENT: A SYSTEMATIC REVIEW.

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Aims: High rates of cannabis use have been reported among individuals being treated for opioid dependence; estimates range from 32% to 66%. Given this high comorbidity, there is a need to examine the extent to which cannabis use impacts treatment for opioid dependence. The present review sought to examine the literature to (1) determine whether cannabis use has an effect on opioid dependence treatment and treatment outcomes and (2) examine other behaviors that are associated with cannabis use among those in treatment for opioid dependence.
Methods: Relevant studies were identified through PubMed, PsycINFO, and citations from identified studies. Six hundred seventy five abstracts were reviewed and 16 articles met inclusion criteria. Included studies examined patients being treated in inpatient and outpatient settings. Rates of cannabis use, treatment setting/modality, treatment outcomes, and other therapy-related behaviors were recorded. Treatment was broadly defined to include both pharmacological and behavioral interventions aimed at reducing illicit opioid use.
Results: Overall, cannabis use was not associated with treatment retention or relapse on opioids or other drugs; however, cannabis use, particularly frequent use, was associated with other behaviors that may have an impact on substance use treatment, such as financial difficulties, acquisitive crime and needle sharing.
Conclusions: This review underscores the importance of monitoring cannabis use in opioid dependence treatment. Although cannabis use may not be associated with relapse on opioids, the associations between cannabis use with needle-sharing and acquisitive crime suggests that cannabis use may be a proxy for other high-risk behaviors. Future studies should examine how cannabis use is related to high-risk behaviors and explore interventions aimed at reducing needle-sharing. In addition, given the increasing prevalence of medical marijuana, research should explore the potential impact that medical use of cannabis may have on opioid dependence treatment.
Financial Support: None.

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PRELIMINARY REPORT OF THC INFLUENCE ON SUBJECT ABILITY TO DISCRIMINATE BETWEEN ACTIVE OPIOID AND PLACEBO IN HUMAN ABUSE LIABILITY STUDY.

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Aims: To assess the impact of THC on subjects' ability to discriminate in HAL study

Methods: To fulfill HAL methodology, subjects with recreational drug experience commonly are recruited and then required to demonstrate they can discriminate between active test opioid and placebo. A positive drug screen serves as a routine exclusion for study participation to eliminate potential bias or risk of pharmacodynamic carryover. However, THC is usually exempt in HAL methodology from this exclusion, in part to improve recruitment and retention of subjects. The impact of THC on pharmacodynamic assessments in drug discrimination is typically considered insignificant but is not well characterized or understood.

In 64 subjects in a single HAL study, investigators examined the potential influence of THC, including quantitative levels where applicable, on ability to discriminate between 20 mg of intranasal oxycodone and placebo.

Results: Of 64 subjects, 31 (48%) were positive for THC prior to drug discrimination. Ten subjects did not complete drug discrimination and were excluded from analysis due to emesis (5), withdrawn consent (3), and inability to complete study meal (2). Of 10 excluded subjects, 60% were positive for THC. The remaining 54 patients completed drug discrimination: 39 passed and were randomized to treatment; 15 did not successfully discriminate. Positive urine drug screen rate for THC was 48.7% for discriminators vs. 40% for non-discriminators (p=0.5650) with corresponding mean urine carboxy-THC concentrations of 705 vs. 417 ng/mL, respectively (p=0.2797).

Conclusions: Successful opioid discriminators were associated with a higher positive THC drug screen rate and mean carboxy-THC urine concentrations when compared to non-discriminators but differences were not statistically significant. The objective measurements of THC do not correlate with subjects' ability to discriminate between active drug and placebo in this intranasal opioid HAL study. Further research is necessary to fully elucidate the influence of THC in HAL studies.

Financial Support: HAL data provided by Collegium Pharma

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THE EFFECTS OF SOCIAL LEARNING ON THE ACQUISITION OF COCAINE SELF-ADMINISTRATION.

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Aims: Social learning models of substance use propose that drug use behaviors are learned, in part, by observing and mimicking the behavior of others. Experimental evidence for social learning in drug use is limited, primarily because of a lack of animal models that permit subjects to observe and mimic the behavior of others during drug self-administration sessions. Recently, we developed custom-built, operant conditioning chambers that permit two rats to be tested simultaneously in the same chamber, thus permitting an examination of social learning on drug self-administration. The aim of this study was to examine the acquisition of cocaine self-administration in three groups of experimentally naïve rats: (1) rats that were tested in isolation, (2) rats that were tested in the presence of another rat that had access to cocaine and had previously been trained to self-administer cocaine (drug-experienced), and (3) rats that were tested in the presence of another rat that did not have access to cocaine (drug-naïve).

Methods: Male rats were reared in isolated or pair-housed conditions for 6 weeks and implanted with intravenous catheters. Pair-housed rats were then randomly assigned to drug-experienced or drug-naïve conditions. In the drug-experienced condition, one rat of each pair was trained to self-administer cocaine in isolation before the reintroduction of its partner. In the drug-naïve condition, one rat of each pair did not have access to cocaine for the duration of the study. For all three groups, the acquisition of cocaine self-administration was measured over 15 consecutive days in the rats with access to cocaine but with no prior operant training.

Results: Relative to isolated control rats, acquisition of cocaine self-administration was facilitated in rats that were tested with a drug-experienced partner; in contrast, acquisition was inhibited in rats that were tested with a cocaine-naïve partner.

Conclusions: These data indicate that the acquisition of cocaine self-administration can either be facilitated or inhibited by social contact. Collectively, these results support a social-learning model of substance use.

Financial Support: DA031725; DA0274855

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WHAT IS THE EVIDENCE FOR HARDENING? TRENDS IN NICOTINE DEPENDENCE IN THE U.S., 2002-2011.

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Aims: There has been considerable interest in determining whether declines in cigarette smoking in the U.S. have resulted in a hardened population of "hardcore" smokers." We analyzed data from the National Survey on Drug use and Health (2002-2011) to study changes in nicotine dependence levels over this time period.

Methods: We used generalized non-linear factor analysis and items from the Nicotine Dependence Syndrome Scale (NDSS) to generate an indicator for dependence that was psychometrically equivalent across years in the study. This approach also allowed us to use Item Response Theory to evaluate changes in the performance of specific NDSS symptoms over time. All analyses were stratified by gender.

Results: As expected, the prevalence of cigarette smoking declined from 2002-2011. The proportion of smokers consuming >25 cigarettes per day also declined. NDSS-based nicotine dependence declined among male smokers, but remained steady among female smokers. However, when the sample was categorized by daily cigarette consumption (0-15, 16-25, >25) we found slight increases in dependence among both male and female smokers who reported consuming 16-25 cigarettes per day. We also found this trend among women who smoked 0-15 cigarettes per day. Smoking to reduce irritability/restlessness became a more accurate marker of severe dependence among men, and smoking to relieve craving became a marker of more severe dependence, and a more accurate marker of dependence, among women.

Conclusions: Overall, we found that dependence may be declining among male smokers, likely due to reduced consumption. However, there may have been increases in dependence among both male and female "pack-a-day" smokers, and dependence itself may have changed to be better identified by withdrawal-related symptoms, suggesting a harder to treat smoking population.

Financial Support: NIDA, PA50DA03394502 (PI: McKee); NIMH, T32MH01423539 (PI: Zhang)

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CARVEDILOL TREATMENT REDUCES COCAINE USE IN METHADONE-MAINTAINED COCAINE USERS.

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Aims: The goal of this study was to test the effectiveness of carvedilol (CAR) for reducing cocaine use in a double-blind, placebo-controlled study. CAR, a mixed alpha1- and beta-adrenergic receptor blocker. We hypothesized that CAR will be more effective than placebo in reducing cocaine use, as measured by cocaine urine results and self-report cocaine use.

Methods: 106 opioid and cocaine-dependent individuals were randomized to one of three treatment groups: placebo (n=34), 25 mg/day CAR (n=37) or 50 mg/day CAR (n=35). Participants attended clinic six days per week to complete weekly assessments, submit thrice weekly urine samples, and ingest study medication under direct observations. The study had 3 phases: methadone induction (2 weeks), treatment (13 weeks) and detoxification (4 weeks). Baseline characteristics of participants were compared using chi-square tests for categorical variables and ANOVA for continuous measures. Continuous and ordinal outcomes were analyzed with a Hierarchical Linear Modeling.

Results: The 3 treatment groups were comparable for basic demographic variables and for the severity of cocaine and other drug use. No significant differences were found for treatment retention across the groups: 56 % of the placebo, 76 % of 25 mg and 66 % of 50 mg CAR group ($p>0.05$). The proportion (SD) of cocaine positive urines during the trial were lower for the 25 mg CAR, 0.5 (0.4), condition, compared to placebo, 0.9 (0.4), or 50 mg CAR, 0.7 (0.3), [$F(2,91)=3.6$, $p<0.05$]. The proportion of heroin positive urines, were not significantly different for the 25 mg CAR, 0.4 (0.4), 50 mg CAR, 0.4 (0.3) or placebo 0.5 (0.3) condition [$F(2,91)=0.8$, $p>0.05$]. The number of days of cocaine abstinence during the past 2 weeks of the trial did not show treatment differences: 7.8 (4.9) for placebo, 8.1 (5.0) for CAR 25 mg, and 6.4 (4.7) for CAR 50 mg [$F(2,82)=0.9$, $p>0.05$].

Conclusions: These findings warrant further clinical trials using CAR with daily doses of 25 mg/day or lower in patients with cocaine dependence.

Financial Support: Supported by the VA MIRECC and NIDA R01 DA019885 grants.

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DECREASED NOREPINEPHRINE TRANSPORTER FUNCTION IN THE ORBITOFRONTAL CORTEX AND ENHANCED COCAINE ABUSE RISK FOLLOWING ADOLESCENT METHYLPHENIDATE TREATMENT IN A RAT MODEL OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Sucharita S Somkuwar[1], Kathleen Kantak[2], Linda P Dwoskin[1]; [1]Pharmaceutical Sciences, University of Kentucky, Lexington, KY, [2]Psychology, Boston University, Boston, MA

Aims: Methylphenidate (MPH) reduces symptoms of Attention Deficit Hyperactivity Disorder (ADHD) by inhibiting dopamine and norepinephrine transporters (DAT and NET) in the medial prefrontal cortex (mPFC) and orbitofrontal cortex (OFC). In the Spontaneously Hypertensive Rat (SHR) model of ADHD, adolescent MPH treatment increased cocaine self-administration, and increased DAT function in mPFC (not OFC) during adulthood compared to VEH control and MPH-treated Wistar-Kyoto (WKY) and Wistar (WIS) controls. Herein, we tested the hypothesis that MPH treatment during adolescence alters NET function in mPFC and OFC of adult SHR.
Methods: SHR, WKY and WIS rats (n=8-9/gp) received oral MPH (1.5 mg/kg) or VEH (1 ml/kg) daily from P28-55. Between P77-91, NET function was determined using in vivo voltammetry. After local ejection of NE (100 μM, with GBR12909, 50 nM), peak amplitude (Amax) and first-order rate constant of uptake (k-1) of NE were recorded. NE uptake rate was calculated as Amax x k-1.
Results: In mPFC, no strain or treatment differences were revealed for NE uptake rate. In OFC, an interaction was obtained for NE uptake rate ($F[2,45]=4.4$, $p<0.05$). NE uptake rate for VEH-SHR (1.3 nM/sec) was 5.2-fold greater than VEH controls and was decreased ($p<0.05$) by MPH during adolescence to control levels.
Conclusions: Increased OFC NET function in SHR may contribute to ADHD-like symptoms and the greater cocaine self-administration compared to WKY and WIS. MPH during adolescence normalized OFC NET function during adulthood, which may contribute to reductions in ADHD-like symptoms. The MPH-induced normalization of OFC NET function suggests that this mechanism does not underlie the enhanced cocaine self-administration in adulthood.
Financial Support: DA011716 and KO Fellowship (SSS)

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OXIDATIVE STRESS, BDNF AND SEVERITY OF CRACK COCAINE USE IN EARLY WITHDRAWAL.

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Aims: An important goal of addiction research is to discover neurobiological markers that could predict severity of addiction and help to determine the appropriate treatment. The aim of this study is to evaluate alteration in oxidative stress markers thiobarbituric acid reactive substances (TBARS) and brain-derived neurotrophic factor (BDNF) among crack cocaine users during early withdrawal and its relationship to severity of drug use.
Methods: longitudinal study with 49 adults crack cocaine users with positive urine cocaine test on their first day of hospitalization at public psychiatric hospital and 49 healthy controls with a negative urine cocaine test from a neighborhood similar to where the cases came from. Blood samples were collected at intake and discharge for the analysis of TABRS and BDNF. Detailed information about crack cocaine use was assessed by the Addiction Severity Index-6th Version (ASI-6). Severity of crack use was estimated using information from age of first crack use, years of crack use and crack rocks used in the previous 30 days.
Results: There is a significant negative correlation between TBARS and BDNF levels at discharged ($r=-0.294$ $p=0.043$) even when controlled for age and days of hospitalization. TBARS levels are positively correlated to severity of crack use ($r=0,304$ $p=0,04$) and BDNF levels are negatively correlated to severity of crack use ($r=-0,359$ $p=0,014$).
Conclusions: TBARS and BDNF blood levels are inversely correlated during early crack cocaine withdrawal, and this is related to the severity of crack use. Therefore TBARS and BDNF could be possible markers of the severity of crack cocaine addiction and cerebral plasticity during early withdrawal.
Financial Support: Secretaria Nacional Anti-Drogas -SENAD
Fundo de Incentivo a Pesquisa e Eventos - FIPE

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THE ROLE OF DISCRIMINATION, ETHNIC IDENTITY, AND ACCULTURATION IN SUBSTANCE USE PATTERNS AMONG MEXICAN ORIGIN TRANSNATIONAL YOUTH.

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Aims: Aims Under the Obama administration, the Department of Homeland Security has deported an average of 400,000 persons per year who are undocumented, many of these are young people who spent a significant amount of time in the U.S. and who can be considered “transnational youth”. For this presentation, transnational youth are defined as young people between the ages of 15 and 24 who have un-willfully moved or were transported to Mexico after living in the U.S. for at least 5 years. This presentation will review extant findings from studies focusing on this growing population in Mexico. A theoretical discussion will highlight the important role of discrimination, acculturation and ethnic identity in affecting the health and mental health status, while delineating how these factors are tied to varying patterns of drug and alcohol use. A theoretical model will be presented accounting for such factors and delineating their role in substance use and abuse.
Methods: This is a theoeretical/commentary abstract.
Results: This is a theoeretical/commentary abstract.
Conclusions: Findings from the limited number of studies suggest the importance of discrimination, acculturation and ethnic identity in influencing the use of drugs and alcohol among transnational youth. These findings point to the need to address the psychosocial and cultural needs of transnational youth through targeted prevention and intervention programs.
Financial Support: Financial Support NIDA training fellowship awarded to second author.

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SEROTONIN (5-HT) 2C RECEPTOR INTERACTION WITH PROTEIN PHOSPHATASE AND TENSIN HOMOLOGUE RESULTS IN DISTINCT PATTERNS OF CORTICAL $ERK_{1/2}$ ACTIVATION.

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Aims: Relapse vulnerability in cocaine dependence is propelled by impulsivity and linked to damped serotonin 2C receptor ($5\text{-}HT_{2C}R$) tone in the medial prefrontal cortex (mPFC). Normalization of $5\text{-}HT_{2C}R$ signaling may be possible by targeting protein:protein interactions with $5\text{-}HT_{2C}R$ as a therapeutic target. Protein phosphatase and tensin homologue (PTEN) is a protein partner of the $5\text{-}HT_{2C}R$ which controls receptor activation states. Interestingly, disruption of the $5\text{-}HT_{2C}R$:PTEN complex by peptide TAT-3L4F potentiates $5\text{-}HT_{2C}R$ signaling and normalizes impulsivity, albeit through an unknown mechanism. The $5\text{-}HT_{2C}R$ is G-protein coupled-receptor through which activation results in extracellular regulated kinases 1&2 ($ERK_{1/2}$) phosphorylation ($pERK_{1/2}$). Here, we test the hypothesis that agonist stimulation of $5\text{-}HT_{2C}R$ and/or pharmacological disruption of the $5\text{-}HT_{2C}R$:PTEN complex will result in distinct patterns of $pERK_{1/2}$ in rodent mPFC.
Methods: Outbred, male Sprague-Dawley rats were administered (i.p.) saline (1 ml/kg), $5\text{-}HT_{2C}R$ agonist WAY163909 (1 mg/kg), TAT-3L4F (10 μmol/kg), or the combination of WAY163909 plus TAT-3L4F. Rats were sacrificed 20 minutes post-treatment and mPFC tissue was collected; nuclear and soluble protein fractions were obtained by differential centrifugation and $pERK_{1/2}$ levels evaluated by immunoblotting.
Results: WAY163909 alone produced an increase in cytosolic and nuclear $pERK_{1/2}$ levels in the mPFC as compared to saline ($p<0.05$). TAT-3L4F alone increased cytosolic $pERK_{1/2}$ ($p<0.05$), but not nuclear $pERK_{1/2}$. The combination of WAY163909 plus TAT-3L4F increased cytosolic $pERK_{1/2}$ but not nuclear $pERK_{1/2}$.
Conclusions: These data suggest that disruption of $5\text{-}HT_{2C}R$:PTEN complex shifts the profile of agonist-induced $pERK_{1/2}$ and represents a neurobiological mechanism which is under interrogation for the development of pharmacological treatments for disorders with disrupted $5\text{-}HT_{2C}R$ signaling.
Financial Support: DA030977

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RISKY BEHAVIORS ON THE ROAD: DO WOMEN AND MEN ACT DIFFERENTLY AFTER DRINKING?

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Aims: To compare differences between female and male drivers regarding select risk factors in two Brazilian cities receiving intervention as part of the Global Road Safety Project.
Methods: A knowledge, attitude and perception (KAP) survey was conducted among drivers in Palmas and Teresina. In October and November 2013, 1,556 face to face interviews were conducted; sampling was done by quotas, according to driver's sex (70.9% male) and age.
Results: The results show that females and males behave differently on the road. Females reported drinking and driving less (41.1% vs 64.9% - p<0.001), and reported being a passenger to someone who had been drinking more (51.9% vs 40.2% - p<0.001). Females who reported binge drinking drove under the influence more than females who had not (55.2% vs 29.1% - p<0.001). Regarding involvement in a road traffic crash while under the influence of alcohol, 11.8% of males reported having this experience in their life as compared to 1.1% of females (p<0.001).
Conclusions: Males represent the most vulnerable road user group due to their being more prone to road traffic crashes and engaging in risky behaviors such as drinking and driving. Similar to global patterns, we found a greater proportion of males engaging in drinking and driving, and experiencing a road traffic crash while under the influence than their female counterparts. However, females self-reported more drink driving associated with binge drinking, and being a passenger of a drunk driver after drinking themselves. These results indicate intervention activities may be tailored to address risky behavior among males, but should also discourage other risk behaviors related to drinking among the general population.
Financial Support: This study is supported by Bloomberg Philanthropies.

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MODULATION OF BEHAVIORAL EFFECTS OF POLYDRUG (COCAINE/HEROIN) MIXTURES BY ALPHA-2 AGONISTS.

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Aims: Noradrenergic alpha-2 agonists have been reported to attenuate opioid withdrawal and proposed as possible anti-relapse medications for cocaine and heroin addiction. We investigated the ability of selected alpha-2 agonists to attenuate behavioral effects of cocaine/heroin mixtures that are associated with addiction liability.
Methods: First, dose-response curves were determined for i.m. clonidine, lofexidine, guanfacine, and brimonidine (UK 14304) in squirrel monkeys using quantitative observational procedures. Next, the modulation of discriminative-stimulus and reinforcing effects of cocaine/heroin mixtures by selected doses of alpha-2 agonists was examined in separate groups of subjects
Results: All drugs produced dose-related sedative-like effects characterized by an increase in species-typical sleep/rest posture and decreases in locomotor activity and environmentally directed behaviors. Impaired balance and muscle relaxation were noted occasionally at the highest doses. Based on their ED min values, the order of potency was: brimonidine (0.1 mg/kg) >lofexidine (0.3 mg/kg) = clonidine (0.3 mg/kg) >guanfacine (1.8 mg/kg). In drug discrimination studies, the discriminative stimulus effects of a cocaine-heroin mixture were not significantly altered by doses of brimonidine, guanfacine or clonidine below those that produced sedative effects and decreased operant responding to <50% of control values. Ongoing self-administration 'choice' studies suggest that daily treatment with clonidine (0.1 or 0.18 mg/kg) leads to a diminution of its sedating effects but continues to produce a >50% decrease in the intake of cocaine/heroin mixtures without consistent modulation of their reinforcing strength.
Conclusions: These data indicate that doses of alpha-2 agonists with behavioral side-effects that diminish over repeated treatment may be useful for in the management of polydrug (cocaine/heroin) addiction.
Financial Support: (supported by DA 031299)

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DIFFERENTIAL EFFECTS OF THE BENZODIAZEPINES ALPRAZOLAM AND OXAZEPAM ON METHAMPHETAMINE-RELATED BEHAVIORS IN RATS.

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Aims: Drug users often combine benzodiazepines with psychostimulants, such as methamphetamine (METH). Previous research has shown that not all benzodiazepines have the same potential for abuse. While alprazolam (ALP) is highly preferred by drug users, oxazepam (OX) has a far lower abuse potential. We hypothesized that METH would induce conditioned place preference (CPP), while OX and ALP would block the METH-induced CPP. We hypothesized that OX and ALP would attenuate METH discrimination.
Methods: CPP was conducted to study the reward potential of the benzodiazepines OX and ALP when combined with METH to simulate polydrug abuse in rats (n=8/group). To determine if ALP and/or OX would alter the subjective effects of METH, we also investigated the effects of these drugs on the discriminative stimulus effects of METH in rats (n=7/group). Rats were trained to discriminate METH (1.0 mg/kg, ip) from saline using a two-lever operant, food-reinforced, drug discrimination design. The effects of ALP (2 and 4 mg/kg, ip) and OX (5, 10, and 20 mg/kg, ip) on METH discrimination were determined by administering these drugs prior to various doses of METH (0, 0.125, 0.25, 0.5, 1, or 2 mg/kg, ip) and then measuring whether the rat pressed the METH- or saline-associated lever. Data were analyzed using one-way ANOVA.
Results: METH produced a CPP, and OX blocked this METH-induced CPP. However, ALP did not block the METH-induced CPP. OX significantly attenuated METH discrimination in rats. However, we found that the high dose of ALP augmented the subjective effects of lower doses of METH.
Conclusions: The results of these experiments suggest that OX and ALP can differentially affect meth-related behaviors. OX attenuates the rewarding properties as well as the subjective effects of METH, while ALP may actually increase the rewarding properties of lower doses of METH. Future research will aim to identify the underlying mechanisms mediating the divergent effects of these benzodiazepines.
Financial Support: No outside funding.

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EARLY EVALUATION OF THE EXPERIENCES AND OPINIONS OF PHARMACISTS TOWARDS THE ONTARIO NARCOTICS MONITORING SYSTEM.

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Aims: Ontario recently implemented a prescription monitoring program which features a unique system of alerts to pharmacists which are triggered when dispensing prescriptions for monitoring drugs based on previous prescription data indicating multiple prescribers, multiple pharmacies, duplicate prescriptions and early or late refills. The purpose of this study was to evaluate the experiences and opinions of pharmacists in relation to the implementation of Ontario's Narcotic Monitoring System, particularly as it pertains to the alert feature.
Methods: An electronic survey was sent to all pharmacists in Ontario 6 months after implementation of the program. The survey included items related to demographics, practice setting, descriptions of significant alert-related patient encounters, positive and negative opinions, and suggestions for improvement.
Results: Of the 972 respondents, 89% (n=867, 52% female) had received an alert since the inception of the program. The majority of pharmacists (90%) indicated receiving the multiple doctors, multiple pharmacies and duplicate drug alerts at least 1-2 days per week. A range of 53%-72% of pharmacists rated most types of alerts as very useful. Pharmacists described over 1,300 significant alert-related encounters, with over one-half triggered when filling an opioid prescription. With most (>70%) of these encounters further communication was made with the patient, pharmacists, and prescribe. Pharmacists indicated the program conferred improved monitoring of prescription drug use, however, conflicts with patients was the most common negative outcome identified (19%).
Conclusions: The new Ontario Narcotics Monitoring System is frequently alerting pharmacists to potentially problematic dispensing patterns that require further inquiry and intervention to resolve. There were generally positive opinions about the system with some limitations identified. Further evaluation is underway to provide program implementers with evidence-based suggestions to optimize program impact.
Financial Support: Canadian Institutes of Health Research

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SEX-RELATED DIFFERENCES IN ORAL OPERANT ETHANOL SELF-ADMINISTRATION IN C57BL/6J MICE.

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Aims: Previous data has revealed sex-related differences in the consumption and effects of alcohol. Mouse models provide a tool for determining the genetic and biological determinants of ethanol use, but there are few operant models of mouse ethanol self-administration. In the absence of flavorants, cues or food/water restriction, this study examined ethanol reinforcement in male and female C57BL/6J mice.
Methods: Following lever training maintained by 0.2% saccharin on an escalating schedule of reinforcement, 15 male and 13 female mice were reinforced with ethanol on a VR5 schedule of reinforcement during weekly, overnight operant sessions for 9 weeks. Active lever pressing resulted in liquid dipper presentation of 0%, 3%, or 15% ethanol in water solution. Food and a water bottle were available ad libitum and water volume consumed was compared against operant fluid intake for an ethanol preference score. Active lever presses, reinforcers earned and ethanol consumed were also measured.
Results: There was a significant interaction of sex with ethanol concentration on ethanol preference ($F=3.407$, $p=0.05$). Both male and female 0% ethanol subjects preferred to drink water from the water bottle over pressing the active lever and drinking from the dipper. Males showed a significant preference for 15% ethanol over water despite having to lever press for ethanol. In females, preference for both 3% and 15% ethanol were observed over water in a dose-dependent fashion. Trends for left shifts in female ethanol intake were also observed for active lever presses ($F=2.94$, $p=0.07$) and total ethanol consumed ($F=2.671$, $p=0.09$).
Conclusions: We developed an operant oral mouse model of ethanol self-administration to assess biological and genetic determinants of ethanol use. Results revealed that females found lower doses of ethanol more reinforcing than male mice, suggesting that females may be more sensitive to ethanol.
Financial Support: This work was supported by grant R01DA031289 to D.H. Brunzell and a pilot project funded through P20AA017828 to M.F. Miles. A.M. Stafford was supported by grant 5T32DA007027 to W. L. Dewey.

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CLIENT PREDICTORS OF TREATMENT COMPLETION USING A U.S. NATIONAL SAMPLE.

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Aims: To identify client predictors of treatment completion for residential and outpatient settings using a national dataset.
Methods: Data were extracted from the 2009 TEDS-D dataset, a federal survey that collects data on all publicly funded drug and alcohol programs in the US, to identify client level predictors of treatment completion for outpatient and residential programs. Approximately 1.6 million cases were included in the analysis using stepwise binary logistic regression performed separately for residential and outpatient programs.
Results: For residential treatment, the strongest predictors for completion were for clients whose primary substance problem was alcohol (OR=1.40), had completed high school (OR=1.21), had full time employment (OR=1.97), and were older than 45 (OR=1.19). The likelihood for non-completion was greatest for opiate users (OR=0.80), Latinos (OR=0.86), African Americans (OR=0.86), those with one or more prior treatment episodes (OR=0.94), females (0.86), and clients living independently (non-homeless) (OR=0.72). For outpatient treatment, there was a similar but not identical pattern. The strongest predictors of program completion were alcohol as primary substance problem (OR=1.56), high school completion (OR=1.12), full time employment (OR=1.25), and being a Veteran (OR=1.10). Those least likely to complete treatment were opiate (OR=0.50) and crack/cocaine users (OR=0.86), African Americans (OR=0.73), Latinos (OR=0.88), those with one or more prior treatment episodes (OR=0.77), and more frequent drug use prior to admission (OR=0.77).
Conclusions: Given that program completion has been found to be one of the strongest indicators related to various positive addiction treatment outcomes (Brorson et al., 2013), identifying predictors of completion and non-completion for residential and outpatient programs can be useful for improving treatment retention. Further research needs to explore additional correlates of program retention and identify how programs can better address clients who are at greater risk of dropout.
Financial Support: No financial support provided.

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EFFECTS OF ENVIRONMENTAL ENRICHMENT ON AMPHETAMINE SELF-ADMINISTRATION UNDER A FIXED-RATIO AND PROGRESSIVE RATIO SCHEDULE FOLLOWING NICOTINE EXPOSURE.

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Aims: Cigarette smoking during adolescence is correlated with an increased likelihood of cocaine or amphetamine use later in life. The present study determined the effects of environmental enrichment on the reinforcing properties of amphetamine following adolescent nicotine exposure using the rodent self-administration model in rats.
Methods: Male Sprague-Dawley rats were received at approximately postnatal day (PND) 21 and placed in one of two environments: an enriched condition (EC) or an isolated condition (IC). From PND 28-35 animals received seven daily injections of 0.4 mg/kg dose of nicotine or saline. Following a 30 day washout period in their respective environments, rats acquired a lever response through food reinforcement. Following the acquisition of the lever press response, all animals underwent catheterization surgery followed by seven recovery days. After recovery, animals acquired self-administration at the 0.1 mg/kg/infusion dose of amphetamine in 60 min self-administration sessions under a Fixed Ratio (FR) 1 schedule of reinforcement. Following acquisition of amphetamine self-administration, a dose effect curve for amphetamine was completed (0, 0.006, 0.01, 0.02, 0.06 mg/kg/inf). Each dose was tested in a random order with three daily sessions at each dose. Finally the animals were switched to a progressive ratio (PR) schedule of reinforcement and a dose effect curve for amphetamine was completed (0, 0.006, 0.01 and 0.06 mg/kg/inf).
Results: Results for FR responding suggest that at the three lowest doses of amphetamine, IC saline- and nicotine-treated rats self-administered more amphetamine than the EC saline- and nicotine-treated rats. Results for the PR schedule found that at the 0.06 mg/kg/inf dose IC-nicotine treated maintained higher breakpoints than all other conditions.
Conclusions: These results indicate that environmental enrichment may decrease the ability of adolescent nicotine exposure to increase the reinforcing effects of amphetamine.
Financial Support: The project was supported by the Creighton College of Arts and Science

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MENTAL HEALTH AND HIV RISK BEHAVIOR AMONG DRUG-USING RURAL WOMEN IN JAIL.

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Aims: Rural women offenders are at high risk for HIV exposure due to the increasing prevalence of injection drug use, as well as limited services. Research on correlates of HIV risk behavior, including drug use and mental health, has primarily focused on women prisoners from urban areas. The purpose of this study is to examine HIV risk behavior (risky sexual activity and injection drug use) by mental health issues among drug-using women in rural jails.
Methods: This study involved random selection, screening, and face-to-face interviews with 103 women from rural jails in one Appalachian state. Analysis focused on the relationship between mental health and HIV risk among this sample of drug-using women.
Results: The majority (79.6%) of women met GAIN criteria for major depressive disorder and about two-thirds endorsed symptoms of generalized anxiety (63.1%) and PTSD (58.3%). Mental health was significantly related to severity of certain types of drug use, as well as risky sexual activity. In addition, for women experiencing anxiety and PTSD, injection drug use moderated the relationship between mental health and risky sexual activity (IRR=1.45, $p<.05$).
Conclusions: Based on these rates of drug use, mental health issues, and the emergence of injection drug use in rural Appalachia, the need to explore the relationships between these issues among vulnerable and understudied populations such as rural women is critical. Due to service limitations services in rural communities, criminal justice venues such as jails provide opportune settings for screening, assessment, and intervention for drug use, mental health issues, and HIV education and prevention.
Financial Support: Research reported was supported by the National Institute on Drug Abuse of the National Institutes of Health under Awards R01DA033866, K02DA35116, and T32DA035200.

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PHYSICIAN SUPPLY FOR THE TREATMENT OF OPIOID USE DISORDERS: THE INFLUENCE OF STATE POLICIES.

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Aims: Buprenorphine is an effective opioid use disorder treatment that can be prescribed in offices only by buprenorphine-waivered physicians. We examined the association between buprenorphine-waivered physician supply, state policies, and community characteristics.
Methods: US Census and Buprenorphine Waiver Notification System data were used to calculate the number of buprenorphine-waivered physicians per 100,000 county residents. State efforts to promote buprenorphine use and state policies supporting buprenorphine use were obtained from state Medicaid office surveys. Multivariate regression models were used to predict the number of buprenorphine-waivered physicians per 100,000 residents at the county level as a function of county characteristics and state policies.
Results: Approximately half of US counties have no buprenorphine-waivered physicians; only 5% of counties have 20 or more waivered physicians. Medicaid reimbursement and other state policies reimbursing for office-based buprenorphine were associated with more buprenorphine-waivered physicians, as was specific state guidance to providers regarding buprenorphine use. Less specific efforts, such as clinical guideline distribution and encouraging methadone programs to advise patients of buprenorphine availability, had no significant impact.
Conclusions: We found a substantial difference in buprenorphine-waivered physicians, with public sector reimbursement and targeted efforts associated with more physicians per capita. State efforts to increase the number of waivered physicians may be an important response to an anticipated increase in demand for effective treatment.
Financial Support: This work was supported by NIDA 1R01DA032881-01A1.

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TASK PERSISTENCE AS A TARGET FOR TOBACCO DEPENDENCE TREATMENT.

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Aims: Most cigarette smokers relapse within 5-10 days of their quit attempt. One potentially modifiable relapse risk factor is "task persistence," the tendency to persist in a difficult task. We previously found that task persistence was positively associated with successful quit attempts in a sample of smokers with and without schizophrenia. The current study reports on an on-going Stage I Behavioral & Integrative Treatment Development project to develop "Persistence Targeted Smoking Cessation" (PTSC), a CBT protocol designed to increase task persistence.
Methods: We recruited adult male and female participants smoking at least 10 cigarettes per day and excluded those regularly using other tobacco products, those with serious mental illness, and those self-reporting problem alcohol or drug use. The PTSC includes core interventions to enhance cognitions, motivation, and behaviors that support increased persistence in general and also related specifically to tolerating distress inherent in smoking cessation. In a pilot randomized trial, PTSC is compared to an established treatment (Clearing the Air, CTA, National Cancer Institute). Both interventions offer 8 weekly individual counseling sessions and use of nicotine lozenge for 12 weeks.
Results: Using an intention-to-treat approach for those reaching their end-of-treatment (n=33) and 3-month post quit-date follow-up dates (n=20), preliminary analyses indicate that difference in abstinence rates between PTSC (44%) and CTA (33.3%) were not statistically significant, but reached trend level significance at three months post quit date (33.0% for PTSC vs. 0% for CTA, $\chi 2(1) = 3.33$, $p = 0.068$).
Conclusions: These pilot data provide preliminary support for a tobacco dependence treatment intervention which combines nicotine lozenges and a cognitive behavioral approach targeting smokers' automatic thoughts and behaviors regarding persistence in general and more specifically related to a quit attempt.
Financial Support: This project was funded by the National Institute on Drug Abuse (R34DA030652) awarded to the first author.

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WITHDRAWN

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PSYCHIATRIC PROBLEMS AND SEX-TRADING AMONG DRUG-USING AFRICAN-AMERICAN WOMEN: DOES FAMILY SUPPORT MATTER?

Danelle Stevens-Watkins, Carl Leukefeld, Carrie B Oser; University of Kentucky, Lexington, KY

Aims: Psychiatric problems, drug use and sex-trading all continue to be viewed as stigmatizing within the African American community and are often not discussed within families. However, psychiatric problems are often co-morbid with substance use and HIV risk behaviors such as sex-trading. The purpose of this study is to explore if family support moderates the relationship between sex-trading and psychiatric problems across multiple waves of data among drug-using African American women (N = 289).
Methods: Data were derived from drug-using African American women in the community, on probation and incarcerated women after community re-entry. Demographics and criminal justice status were included in the multivariate models. The mean age of study sample was 36.32 (SD = 9.67). The average years of education was 11.41 (SD = 2.04). While controlling for psychiatric problems at baseline, it was hypothesized sex-trading would increase the likelihood for experiencing psychiatric problems 6 months later and family support would moderate the relationship between sex-trading and psychiatric problems.
Results: The women who reported sex-trading at baseline were over 5 times more likely to experience increased psychiatric problems six months later (OR = 5.19, $p < .01$). For every one unit increase in perceived family support the women were 14% less likely to have participated in sex-trading (OR = 0.86, $p < .05$). To test for moderation, results demonstrated that the interaction term was not significant. Being in prison was associated with increased psychiatric problems 6 months after community re-entry compared being on probation and in the community.
Conclusions: With family support being a significant factor, the involvement of close family members in the treatment of drug-using women with psychiatric problems could be beneficial in reducing risky behaviors. The assessment and treatment of psychiatric problems among drug-using women could reduce their risky sexual behavior, particularly for women in prison nearing community re-entry.
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ATTENUATED INSULAR AND FRONTOCINGULATE DECISION-MAKING RELATED ACTIVATION DURING AN AVERSIVE INTEROCEPTIVE STATE IN METHAMPHETAMINE-DEPENDENT INDIVIDUALS.

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Aims: Stimulant dependent individuals often make drug-taking decisions when they do not feel well. Yet few studies have examined the influence of an aversive state on decision-making related neural processing. We investigate brain activation to action-outcome contingencies during an aversive interoceptive challenge in methamphetamine users using functional magnetic resonance imaging (fMRI).
Methods: Abstinent methamphetamine dependent inpatients (MD; n=20) and healthy comparison subjects (CTL; n=22) performed a two-choice prediction task at three fixed error rates (20%=reward, 50%=uncertainty, 80%=punishment) while anticipating and experiencing episodes of inspiratory breathing load during fMRI. Participants rated breathing load unpleasantness/intensity using visual analog scales (VAS).
Results: MD exhibited lower anterior insula (AI) and inferior frontal gyrus (IFG) activation than CTL across trials. MD also showed lower posterior insula (PI) and anterior cingulate cortex (ACC) activation than CTL during breathing load independent of error rate. For the crucial error rate by interoception interaction, MD displayed lower dorsal ACC activation to punishment than CTL during breathing load. Within MD, higher VAS unpleasantness was linked to lower dorsal ACC activation to punishment during loaded breathing.
Conclusions: AI/IFG attenuations in MD are suggestive of a global decision making deficit, reflecting reduced resources allocated to the processing of action-outcome contingencies. In contrast, PI/ACC reductions in MD appear specific to impairments in registering and evaluating interoceptive experiences. Taken together, inadequate activation of brain areas that are important for regulating how one feels during an aversive interoceptive state may be the neural basis for poor decision-making by MD individuals.
Financial Support: NIDA 5P20DA027843-04

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EVIDENCE OF GENDER-SPECIFIC TELESCOPING EFFECTS IN CHRONIC, REGULAR HEROIN USERS.

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Aims: Addiction literature suggests the possibility of gender-specific telescoping effect whereby females initiate substance use later in life, but escalate to dependence more quickly, "catching" their male counterparts and exhibiting worse substance use-related outcomes. This study retrospectively investigated the presence of a gender telescoping effect in chronic, regular heroin users.
Methods: Chronic, regular, non-treatment seeking heroin using adults (N=451; aged 18-55 yrs) were screened for laboratory-based research studies. The modal participant in this sample was a 43 year old African American (60.7%) male (70.7%). Heroin-related adverse consequences were assessed using a 21-item questionnaire based on DSM-5 heroin use disorder criteria.
Results: Analyses of variance revealed females' first heroin use occurred later than males, $F(1,450)=4.39$, $p<.05$; M=24.8 [f] vs. 23.1 [m] yrs, although gender was not related to age at first regular heroin use ($p=.12$). Among females, younger onset of regular heroin use was associated with more heroin use-related consequences, $F(1,130)=17.26$, $p<.001$, but not lifetime number of attempts to quit heroin. Among males, younger onset of regular heroin use was associated with more consequences and quit attempts, $F(1,316)=10.76$, $p<.001$, $F(1,313)=6.77$, $p<.01$, respectively.
Conclusions: These findings suggest a gender-specific telescoping effect in which females initiated heroin use later but escalated to regular use more quickly, which may indicate a unique vulnerability to heroin dependence. Younger onset of regular use was associated with more lifetime consequences in both genders, but was only related to more quit attempts in males. Taken together, these findings highlight differential heroin trajectories by gender and illustrate the relevance of gender for treatment.
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INFLUENCE OF BUPROPION, NALTREXONE AND BUPROPION+NALTREXONE ON METHAMPHETAMINE SELF-ADMINISTRATION IN HUMANS.

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Aims: Clinical research shows that monotherapies generally have little efficacy for managing methamphetamine use disorders. Two drugs, bupropion and naltrexone, have produced modest reductions in methamphetamine use clinically. Whether combining these drugs would result in greater reductions in methamphetamine taking relative to either drug alone is undetermined. This study examined the influence of bupropion, naltrexone and bupropion+naltrexone on methamphetamine self-administration in humans.
Methods: Seven subjects reporting recent illicit stimulant use completed a placebo-controlled, crossover, double-blind study in which the reinforcing effects of intranasal methamphetamine (0, 10 and 30 mg) were assessed during maintenance on placebo, bupropion (300 mg/day), naltrexone (50 mg) and bupropion+naltrexone. A battery of subjective and physiological measures was also completed for each dose condition. Data were analyzed using repeated-measures ANOVA with the hypothesis that the bupropion+naltrexone combination would attenuate the effects of methamphetamine to a greater degree than either constituent drug alone.
Results: Methamphetamine maintained responding and produced prototypic subjective and physiological effects (e.g., increased ratings of Good effects, elevated heart rate). Bupropion, naltrexone and the combination were all well tolerated and generally devoid of effects. No maintenance condition reduced methamphetamine self-administration or systematically altered the subjective effects of methamphetamine. Maintenance doses accentuated the cardiovascular effects of methamphetamine.
Conclusions: These outcomes demonstrate the robust behavioral effects of methamphetamine, as well as the resistance of methamphetamine taking to pharmacological manipulation. Future work with this combination should test multiple doses of the maintenance drugs under different behavioral arrangements in a larger sample.
Financial Support: Supported by a grant from NIDA (R01 DA 025032; PI: CRR).

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BUFFERING EFFECTS OF MORAL IDENTITY ON THE LINKS BETWEEN PEER RELATIONSHIP QUALITY AND PROBLEM BEHAVIORS.

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Aims: Aims: There is much interest in understanding factors that protect individuals from substance use and risky sexual behaviors. Relationships with peers can have positive or negative influences on youths' outcomes and peer influences may be moderated by dispositional characteristics. Moral developmental scholars have suggested that youth who exhibit strong moral identity may be less prone to problem behaviors. This study examined the potential buffering effects of moral identity (i.e., a belief that morals are tied to one's sense of self), on the links between peer relationship quality and drug and sexual risk outcomes. We expected that the relations between both peer negativity and positivity and adolescents' problem behaviors would be weaker for those with high levels of moral identity.
Methods: Methods: College students (N= 303, M age = 18.71, 62.7 % female) completed measures of peer relationship quality, moral identity, substance use, and risky sexual behaviors.
Results: Results: Path analyses demonstrated that greater peer positivity was associated with more alcohol use, binge drinking, and more sexual partners ($\chi 2 = 14.96$; CFI = .96; RMSEA =.23). Greater peer negativity was associated with more marijuana use and tobacco use ($\chi 2 = .00$; CFI = 1.00; RMSEA =.00). Moreover, the links between peer relationship quality and substance use were moderated by moral identity. Findings suggest that moral identity buffers the negative associations between the quality of peer relationships and drug use, such that the relations are weaker for those individuals who exhibited high levels of moral identity.
Conclusions: Conclusions: Findings demonstrate the importance of studying protective factors, specifically moral identity, that reduce drug use and risky sexual behaviors. Discussion will focus on the relevance of moral dispositional characteristics in understanding the relation between peer influence and youth drug use and risky sexual outcome.
Financial Support: Financial Support: Mizzou Advantage grant from the University of Missouri.

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AEROBIC EXERCISE DECREASES SPEEDBALL SELF-ADMINISTRATION IN FEMALE RATS.

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Aims: Preclinical studies have reported that aerobic exercise, in the form of treadmill or wheel running, reliably decreases the positive reinforcing effects of psychomotor stimulants and opioids. To date, preclinical studies have only examined the effects of exercise on responding maintained by individual drugs and not by combinations of multiple drugs. This limits the translational appeal of these studies because polydrug abuse is common among substance abusing populations. The purpose of this study was to examine the effects of aerobic exercise on the positive reinforcing effects of speedball, a combination of cocaine and heroin that is frequently encountered in intravenous drug abusing populations.
Methods: Female rats were obtained at weaning and assigned to sedentary or exercising conditions. Sedentary rats were housed in standard cages that permitted no exercise beyond normal cage ambulation; exercising rats were housed in similar cages with an activity wheel. After 6 weeks, rats were implanted with intravenous catheters and trained to self-administer cocaine, heroin, and dose combinations of cocaine and heroin (i.e., speedball) on a progressive ratio schedule of reinforcement.
Results: Doses of speedball maintained greater levels of responding than corresponding doses of cocaine and heroin alone. Importantly, breakpoints maintained by cocaine, heroin, and speedball were lower in exercising rats than sedentary rats.
Conclusions: These data indicate that exercise decreases the positive reinforcing effects of speedball and suggest that exercise may reduce the abuse of drug combinations that have traditionally been resistant to treatment.
Financial Support: NIH Grants R01DA031725 and R01DA0274855

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WIYHDRAWN

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EFFECTIVENESS OF AMBASSADOR PLUS NAVIGATOR VS. NAVIGATOR ALONE TO ENROLL CURRENT DRUG USERS IN HEALTH STUDIES.

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Aims: Any current drug use often excludes people from health studies, regardless of whether or not drug interactions would medically preclude participation. With 21% of youth 18 to 25 years of age and at least 7 % of adults over 25 years of age currently using illicit drugs, studies that unnecessarily exclude drug users limit the generalizability of their results.
Methods: With the aim of increasing current drug users' participation in research, the Transformative Approach to Reduce Research Disparities towards Drug Users (NIDA funded, Cottler PI) randomized users and non-users to an Enhanced Navigation (NAU+) or Navigation as usual (NAU) intervention. In NAU+, participants receive enhanced, one-on-one interaction with an Ambassador, who guides them throughout the research process, including transporting and accompanying them through study enrollment and participation. NAU participants are navigated to a study coordinator for possible study participation, but do not receive enhanced, personalized assistance throughout the entire research process. As of November 2013, 505 adults 18 years of age and older were randomized to NAU (n=252) or NAU+ (n=253); 377 completed a 90 day follow-up interview (NAU=187; NAU+=190).
Results: Women (NAU 57%; NAU+ 50%) and African Americans were in a slight majority (NAU 54%; NAU+ 56%), with a mean age of 43. Lifetime use of illicit drugs or misuse of prescription drugs was common in the sample (NAU 48%; NAU+ 46%), as was alcohol abuse or dependence (NAU 27%; NAU+ 25%).
Among those with completed 90 day interviews, 30% of NAU+ participants compared to 15% of NAU were enrolled in 1+ research study (p=.0005). Ambassadors increased enrollment among both drug users (27.3% vs 18.2%; p=.1783) and non-drug users alike (31.9% vs 12.7%; p=.0006).
Conclusions: Navigating drug users to research helps to diversify participant sample pools. Our findings demonstrate that Ambassadors can further improve the effectiveness of the enrollment intervention beyond navigation.
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ANCILLARY TREATMENT USE IN THE STAGE II COMMUNITY-BASED WOMEN'S RECOVERY GROUP THERAPY TRIAL.

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Aims: In a Stage 2 trial of the single-gender Women's Recovery Group (WRG), women randomized to the WRG (n = 52) or mixed-gender Group Drug Counseling (GDC; n = 48), and men assigned to GDC (n = 58) had clinically significant reductions in mean days of substance use at end of treatment and 6 month follow-up. Groups were implemented in a rolling format consistent with community practice and participants could engage in treatment as usual (excluding other substance abuse group therapy during the 12-week group treatment). We investigated gender and group differences in ancillary treatment utilization at baseline, end of group treatment, and 6 month post-treatment follow-up.
Methods: Participants ≥18 years were included if they were substance dependent and used substances in the past 60 days. Ancillary treatment was assessed using the Treatment Services Review and Monthly Self-Help Questionnaire. For self-help groups, participants were asked to report on their experiences in the "last month."
Results: Participants engaged in self-help groups an average of 9 days (SD = 9.4) at baseline, 7 days (SD = 9.5) at the end of treatment, and 6 days (SD = 8.9) at 6-month follow-up. There were no group or gender differences in self-help attendance. Compared to men, women were more likely to be engaged in individual psychotherapy at baseline (61% vs. 45%; $\chi 2(1) = 3.88$, $p<.05$), at end of treatment (80% vs 54%; $\chi 2(1) = 10.14$, $p<.01$), and 6-months post treatment (73% vs. 46%; $\chi 2(1) = 9.87$, $p<.01$). There were no group differences in psychotherapy utilization. Few participants reported engagement in other group therapies or seeing substance dependence counselors.
Conclusions: The most frequently used ancillary treatments were self-help groups and individual psychotherapy. Consistent with the literature, women were more likely to attend psychotherapy compared to men.
Financial Support: NIDA R01 DA015434 and K24 DA019855

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POORER PRE-POTENT RESPONSE INHIBITION IN COCAINE-DEPENDENT PATIENTS VS. HEALTHY CONTROLS DURING AN AFFECT-CONGRUENT GO-NOGO TASK.

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Aims: Our laboratory previously introduced an affectively congruent Go-NoGo task (GNG) using affective stimuli with inherent ecological validity (Go = "positive" stimuli; NoGo = "negative" stimuli), and showed adequate task validity and reliability in individuals at-risk for substance addiction. No prior studies have compared GNG performances between cocaine-dependent (CD) and healthy matched-control (HMC) subjects. In the current study, we compare the prepotent response inhibition performance of these groups using our affectively congruent GNG.
Methods: CD (n=48) and HMC (n=18) underwent three conditions of GNG trials varied by difficulty levels: ratio of NoGo to Go stimuli as 12.5%, 25% and 33%. Prior to task, CD spent approximately 4-7 days in a controlled therapeutic setting to ensure stable, cocaine-free state. The number of commission and omission errors were assessed as outcome measures.
Results: Repeated-measures analysis of variance of commission error scores yielded main effects of group (CD>HMC) ($p=0.03$) and degree of difficulty (12.5%>25%>33%) ($p<0.001$). The interaction between these factors was also significant ($p=0.03$). Post-hoc analyses of commission error scores revealed that the two groups differed only at the least difficult 33%, level. A comparison in omission scores showed a significant main effect of difficulty level (12.5%>25%>33%) ($p=0.02$), but no group effect ($p=0.06$).
Conclusions: CD committed more errors than HMC when they attempted to inhibit a prepotent response. Only at the least difficult level, was the performance of CD and HMC groups significantly different. As expected, both commission and omission errors increased as task difficulty increased. Prepotent response inhibition marker may represent important phenotypic behavioral indicator of chronic cocaine use. 33% difficulty level may be potentially useful to predict drug initiation, addiction and relapse.
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LONG-ACTING INJECTABLE NALTREXONE INDUCTION: A RANDOMIZED TRIAL OF OUTPATIENT OPIOID DETOXIFICATION WITH NALTREXONE VS. BUPRENORPHINE.

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Aims: Antagonist therapy for opioid dependence with naltrexone, available in long-acting injectable form, represents an important but underutilized treatment option. The aims of this study are to develop procedures for outpatient detoxification and to compare induction rates onto injectable naltrexone (XR-NTX) between groups receiving naltrexone-assisted vs. buprenorphine-assisted outpatient detoxification.
Methods: Opioid-dependent participants seeking treatment were randomized into 2 groups for short-term outpatient opioid detoxification. One group received a 7-day buprenorphine taper, followed by a 7-day long washout and an injection of XR-NTX. A second group received a single day of buprenorphine, followed by a washout day and 4-day oral naltrexone taper and an injection of XR-NTX. Following induction, participants received behavioral therapy for 4 weeks
Results: To date, 79 participants (65% white, 86% male, 34% prescription opioid users) have entered the study and were randomized to naltrexone (n=53) or buprenorphine (n=26) arm. 51% of participants in the naltrexone arm and 46% in the buprenorphine arm have been successfully inducted onto XR-NTX ($p=.69$). 50% of participants in the naltrexone arm and 36% in the buprenorphine arm completed Week 5 ($p=.25$) and received a second XR-NTX injection.
Conclusions: The data from this study suggests that oral naltrexone is an important alternative medication useful in the opioid detoxification process. Participants treated with naltrexone during detoxification had comparable outcomes with those in the buprenorphine-assisted detoxification in becoming inducted onto XR-NTX. At least half of the patients undergoing oral naltrexone-assisted outpatient detoxification completed induction onto XR-NTX. These results suggest initiation of XR-NTX on an outpatient basis is a clinically viable treatment option that may be attractive to many patients and providers.
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GENETIC BACKGROUND INFLUENCES THE CHANGE FROM THE DISCRIMINATIVE STIMULUS TO THE REWARDING EFFECTS OF PSYCHOSTIMULANTS IN RATS.

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Aims: The discriminative stimulus effects of psychostimulants are closely associated with their rewarding effects. It has been shown that Lewis (LEW) rats are more sensitive to the behavioral effects of psychostimulants than Fischer 344 (F344) rats. However, little information is available regarding the genetic background on the discriminative stimulus effects of psychostimulants. Therefore, the present study was designed to investigate the possible similarities between the sensitivity to the production of discriminative stimulus effects and the rewarding effects of psychostimulants in LEW and F344 rats.
Methods: Drug discrimination, conditioned place preference, and in vivo microdialysis studies by using LEW and F344 rats were conducted based on our previous reports.
Results: In the conditioned place preference paradigm, psychostimulants produced strong rewarding effects in LEW rats, while no significant effects were seen in F344 rats. On the other hand, there was no difference in the discriminative stimulus effects as well as dopamine-releasing effects from the nucleus accumbens after psychostimulants administration between LEW and F344 rats. Furthermore, we found that the number of astrocytes in the nucleus accumbens was almost 3 times larger in LEW rats than those in F344 rats.
Conclusions: These results suggest that the genetic background may influence the change from the discriminative stimulus effects of psychostimulants to their rewarding effects as the postsynaptic event in the nucleus accumbens.
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COFFEE AND ENERGY DRINK USE IN COLLEGE FRESHMEN: IS TROUBLE BREWING?

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Aims: Historically, daily coffee use was associated with heavy alcohol use and problems (Hull et al., 2011). More recently, caffeine-containing energy drink (e-drink) use has escalated in college students, and e-drinks have been linked to alcohol dependence, marijuana use and risky sexual behaviors (e.g., Arria et al., 2011). The present study compared rates of alcohol/other drug use and problems in 3 groups of freshmen: those consuming coffee + e-drinks (C+E); those consuming coffee but no e-drinks (C) and those consuming neither substance (NoCE).
Methods: Subjects were N=1,953 freshmen at an urban university who completed a 30-min on-line survey. Survey domains included: demographics, alcohol and other drug use (including caffeine), personality and family history (Spit for Science project*). The sample was 39% male; 52% Caucasian and 20% Black. The 3 caffeine use groups included: C+E (N=144) C (N=883) and NoCE (N=926) Alcohol, tobacco and other drug use and family history variables were compared across the 3 caffeine use groups controlling for race and gender, using a logistic regression model with post-hoc comparisons.
Results: Relative to NoCEs, C+Es were significantly more likely to endorse 8 of 9 alcohol use disorder diagnostic symptoms. Further, C+Es endorsed 6 of the 8 alcohol symptoms at higher rates than Cs (all $p<.05$). For other drugs, there was also a significant difference between the 3 groups, with C+Es having the highest rates of use (6+ times) of cannabis, sedatives, stimulants, cocaine and opioids (all $p<0.002$). Cigarette smoking (100+ cigs) followed the same pattern (31% E+C; 11% C and 7% NoCE; $p< .0001$). Finally, E+Cs were more likely to report maternal alcohol and drug and paternal drug problems than Cs and NoCEs (all $p<.05$).
Conclusions: While findings affirmed the association between caffeine use and alcohol/other drug use and problems, the relationship was strongest in students consuming both coffee and energy drinks. Results should inform future prevention and intervention efforts.
Financial Support: NIH R37 AA011408* and RO1 DA026091

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LOSS OF SEROTONIN (5-HT) 2C RECEPTOR (5-HT$_{2C}$R) TONE IN THE VENTRAL TEGMENTAL AREA MODULATES COCAINE-RELATED BEHAVIORS.

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Aims: The mesocorticolimbic dopamine system is known to mediate the hypermotive and reinforcing effects of cocaine. Serotonergic afferents to the VTA regulate dopamine transmission through the 5-HT$_{2C}$R which exerts an overall inhibitory impact on VTA function. Although understudied, a few reports identified a role for VTA 5-HT$_{2C}$R signaling such that intra-VTA microinfusion of a 5-HT$_{2C}$R agonist has been shown to decrease cocaine-evoked hyperactivity and cocaine self-administration. Here, we employ a virally-mediated genetic knockdown strategy to expand upon these observations and test the hypothesis that diminished VTA 5-HT$_{2C}$R tone alters cocaine-related behaviors.
Methods: Male Sprague-Dawley rats were evaluated for basal motor activity and cocaine-evoked hyperactivity following genetic knockdown of 5-HT$_{2C}$R in the VTA. We assessed hyperactivity after an injection of cocaine (10 mg/kg, i.p.) in VTA 5-HT$_{2C}$R knockdown and control rats. Rats were then trained in daily three-hour sessions to self-administer a low dose (0.25 mg/kg/inf) of cocaine on an FR1-5 schedule; the cocaine dose-response (0.05, 0.125, 0.25 and 0.75 mg/kg/inf) relationship was then evaluated to interrogate differences in sensitivity to cocaine.
Results: Rats with genetic knockdown of the 5-HT$_{2C}$R in the VTA displayed enhanced cocaine-evoked hyperactivity ($p<0.05$) but no difference in basal locomotion relative to control rats. There was no difference in acquisition of cocaine self-administration or infusions earned during the cocaine dose-response sessions between VTA 5-HT$_{2C}$R knockdown and control rats.
Conclusions: These data suggest reduced VTA 5-HT$_{2C}$R tone confers an increased sensitivity to the hypermotive response but not the reinforcing properties of cocaine. Investigation into the role of VTA 5-HT$_{2C}$R tone on other cocaine-related behaviors, such as motivation to respond for cocaine or cocaine cue reactivity, are underway and will provide further insight into which facets of responsivity to cocaine are modulated by 5-HT$_{2C}$R function in the VTA.
Financial Support: DA035620, DA06511, DA024157, DA033935, DA033374

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EFFECTS OF INTRAMUSCULAR AND ORAL BUSPIRONE ON PHYSIOLOGY AND BEHAVIOR IN MONKEYS.

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Aims: Buspirone has multiple actions in the brain including dopamine (DA) D2-like receptor antagonism. Recent data suggest that buspirone has higher affinity at the DA D3 receptor (DAD3) compared to the DA D2 receptor (DAD2) subtype; DAD3 has been a target for medications to treat drug addiction. One behavioral assay that has been used to assess DAD3 and DAD2 involves administration of the D2-like agonist quinpirole (QUIN). QUIN elicits yawning and the ascending limb of the dose-response curve is thought to be DAD3 mediated, while higher doses of QUIN result in fewer yawns and in hypothermia; the latter is thought to be DAD2 mediated. The goal of this study was to examine, in separate groups of monkeys, the effects of buspirone administered by different routes on behavior (QUIN-elicited yawning) and physiology (QUIN-induced hypothermia).
Methods: In drug-naïve male rhesus monkeys (n=3), QUIN (0.01-0.3 mg/kg, i.m.) elicited yawning that was characterized as an inverted U-shaped function of dose, with peak yawning following 0.1 mg/kg QUIN. In a second study, drug-naïve female cynomolgus monkeys (n=4) were surgically implanted with indwelling telemetry transmitters (D70-PCT; Data Sciences International, St. Paul, MN). QUIN (0.1 mg/kg, i.m.) induced significant hypothermia.
Results: Irrespective of route, buspirone (0.1, i.m. and 0.3-1.0 mg/kg, p.o.) attenuated 0.1 mg/kg QUIN-elicited yawning. Intramuscular (0.1-0.56 mg/kg) but not oral (1.0-5.6 mg/kg) buspirone attenuated QUIN-induced hypothermia.
Conclusions: The present data support the hypothesis that oral buspirone is primarily a DAD3 antagonist. If DAD3 is a viable target for addiction medications, then additional studies using oral buspirone are warranted.
Financial Support: DA012460 and DA010584

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LOWER OXIDATIVE STRESS IN UMBILICAL BLOOD CORD OF NEWBORNS EXPOSED TO CRACK DURING PREGNANCY.

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Aims: The use of crack-cocaine is a major health concern in several countries. Among its users, pregnant women and their newborns, exposed to crack-cocaine intrautero, deserve special attention. One of the toxic mechanisms of crack-cocaine consists of oxidative stress (OS), which plays an important role in the embryonic development, neonatal and pregnancy-related disorders. Little is known about OS in babies exposed to crack-cocaine during pregnancy. The aim of this study was to compare the levels of OS in newborns exposed to crack during pregnancy (EN) and non-exposed newborns (NEN).
Methods: A cross-sectional study in which the levels of lipid peroxidation and oxidative damage to proteins, measured, respectively, by Thiobarbituric Acid Reactive Substances (TBARS) and carbonil in the umbilical cord blood -UCB) were compared among 48 EN and 83 NEN. Demographic data, presence of psychopathology and use of other substances were assessed in the mothers.
Results: After adjustment for maternal psychopatology, newborn weight and alcohol use by mothers, the mean levels of TBARS were significant lower in the group of EN (26.64, CI95%=20.35-34.88) in comparison to NEN (92.99, CI95%=90.48-107.44, P<0,001). There were no significant differences on carbonil levels between groups (0.02065, 0.001160-0.344170 in EN, vs 0.0189, 0,0076-2,17091 in NEN, P =0.33).
Conclusions: The exposed babies had lower OS, probably induced by Cocaine and Amphetamine Regulated Transcript (CART), which stimulates antioxidant routes. Since both low and high OS are associated to embryotoxicity, the long term effects of these very early adjustments require further investigations.
Financial Support: This study was funded by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS) e do Fundo de Incentivo à Pesquisa e Eventos (FIPE) do Hospital de Clínicas de Porto Alegre (HCPA). All Brazilian institutions.

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METHAMPHETAMINE SELF-ADMINISTRATION IN RATS IS DIMINISHED BY WHEEL ACCESS IN THE PRIOR 22 HOURS.

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Aims: Prior studies found that a 6 week interval of access to an activity wheel reduces the intravenous self-administration of cocaine and methamphetamine in rodent models. Such models confounded prior wheel exposure with the acute effects of wheel activity in the home cage during self-administration training. A recent study found that ~22hrs of wheel access prior to sessions, without any extended prior exposure, was sufficient to reduce cocaine self-administration in a between-groups design. The present study sought to determine if ~22hr access to a wheel reduces methamphetamine (MA) self-administration.
Methods: . Groups of male Sprague Dawley rats were trained to stably self-administer MA (0.05 mg/gk/infusion, i.v.) and then subjected to wheel access/no access conditions when in the vivarium. Intake of MA was significantly lower on sessions following ~22 hrs of access to the wheel compared with sessions which followed ~22 hrs of normal housing. Effects of the wheel were observed within-subject in an ABAB design as well as between groups.
Results: Metamphetamine self-administration was reduced in sessions following 22 hours of wheel access both within and between subjects.
Conclusions: These data provide evidence that a suppressive effect of wheel activity that had previously been attributed to sustained, multi-week wheel access is instead due to acute wheel activity in the day prior. Thus, brain plasticity mechanisms that require 6 weeks of chronic activity to produce are unlikely to be related to the suppressive effect of activity on drug self-administration. This study also has important implications for using exercise as an adjunct to human drug cessation therapy because an extended interval of escalated activity may not be required. The study also shows that consistent daily activity may be required for maximum effect.
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BRAIN BIOMARKERS OF ALCOHOL ABUSE AT AUTOPSY.

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Aims: Identification of chronic excessive alcohol consumption in living and deceased individuals is a fundamental task in forensic pathology, because antemortem reports are often unreliable. Alcohol abuse is widely recognized as an important background factor in motor vehicle accidents, occupational accidents, homicides and suicides. In clinical practice, several blood markers are used, but these are not applicable for identifying alcohol exposure at autopsy. Carbohydrate deficient transferrin in serum is a reliable indirect marker of recent alcohol use, but the application to postmortem brain measurement is problematic. We studied phosphatidylethanol (PEth) and ethyl glucoronide (EtG), two direct biomarkers of ethanol consumption. PEth is an abnormal phospholipid formed only in the presence of ethanol. EtG is a direct minor metabolite of ethanol that serves as an antemortem marker of alcohol ingestion.
Methods: PEth and EtG were analyzed in social drinkers who died suddenly (n=12) and heavy drinkers (n=24) who by report were either abusing alcohol at the time of death or recently abstinent with negative blood alcohol concentrations (BAC) at autopsy. Human brain tissues were obtained and frozen at -80° C until solid phase extraction. The concentration of PEth and EtG in the cerebellum was determined using LC-MS/MS (Agilent 6460). The limit for detection of PEth and EtG were 4 ng/g and 3 ng/g, respectively.
Results: In social drinkers that had negative BAC at autopsy, 8 to 9 out of 12 subjects tested positive for PEth (13.1 –1307.2 ng/g) and/or EtG (6.0 – 57.0 ng/g). In alcoholics who had negative BAC at autopsy, 11 out of 12 tested positive for PEth (5.93 ng/g – 9887.0 ng/g) and 10 out of 12 for EtG (19.5 ng/g – 402.4 ng/g). The mean concentration of PEth was 3012.41 +/- 683.7 ng/g in the 12 active alcoholics (BAC 0.24 +/- 0.04 %). For the chronic alcohol abusers with negative BAC, the biomarker sensitivity for PEth and EtG was 91% and 83%, respectively.
Conclusions: EtG and PEth are useful surrogate markers for detecting excessive alcohol drinking, providing a longer detection window and good sensitivity.
Financial Support: NIDA DA06227-19.

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A TRANS-GENERATIONAL RIPPLE: HOW A PUFF DURING EARLY DEVELOPMENT LED TO A GLOBAL HUFF IN MICRORNA PROFILES AS WELL AS GRAND-OFFSPRING ADDICTIVE BEHAVIOR IN *CAENORHABDITIS ELEGANS*

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Aims: We employed *C. elegans* to study the effect of post-embryonic nicotine exposure on parental global miRNA expression profiles and to investigate possible trans-generational alterations in behavior.
Methods: Nicotine treatment was limited to N2 (strain) hermaphrodites of the F0 generation during larval (~30 hours) period after which worms were washed and transferred to a fresh NGM plate. Parent L4 larvae were collected for qRT-PCR analysis for all of 231 miRNAs. Behavior was analyzed across three generations: F0, F1, and F2. MicroRNA-target predictions and analyses were based on mirSOM, GOrilla, and DAVID. WormLab software (MBF) was used to analyze worms' behavior. Three and four biological replicates were used per treatment group for molecular and behavior analyses (2000 and 20 worms/replicate, respectively). Statistical significance was computed using ANOVA and chi-square test.
Results: Nicotine significantly altered the expression patterns of 40 miRNAs in the parent F0 generation. Select miRNAs (mir-80) were predicted to regulate key nicotine-induced proteins (e.g. fos-1). We inferred that miRNAs as a system mediates "regulatory hormesis", manifested in biphasic behavioral changes. Indeed, post-embryonic parental nicotine exposure was associated with changes in sinusoidal locomotion, speed, and body bends in L4 larvae in all of F0, F1, and F2 generations, the latter of which were never exposed to nicotine and modeled withdrawal.
Conclusions: Our study is the first to reveal that nicotine addiction is heritable using *C. elegans* as a model organism. We hypothesize that this trans-generational effect might be linked to changes in global miRNA profiles. Our results offer new insights that underscore the sensitivity of early development stages, with hope to spread more awareness to avoid nicotine exposure, especially at a young age.
Financial Support: This project is partially supported by Grant Number R03DA032515 from the National Institute on Drug Abuse.

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INCREASING PSYCHIATRIC COMORBIDITY IN RECENT SMOKING BIRTH-COHORTS.

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Aims: Smoking, increasingly recognized as a hazardous exposure, has declined in prevalence and become a more socially deviant behavior. Thus, persons initiating smoking in recently-born cohorts may differ from those who initiated smoking decades ago in terms of personality and comorbidity. We hypothesized that more recently-born cohorts of smokers would have greater lifetime rates of behavioral psychopathology than smokers from earlier cohorts, who entered the ages of risk for smoking during eras when tobacco use was more normative.
Methods: Participants (N=30,953) from the National Epidemiologic Survey on Alcohol and Related Conditions were classified into one of 6 birth-cohorts (born 1930s-1980s) and 3 smoking groups (nonsmokers, never dependent, and ever dependent). Diagnoses including nicotine dependence, drug (DUD) & alcohol (AUD) use disorders, major depression (MD), attention deficit hyperactivity disorder (ADHD), and antisocial personality disorder (APD) were measured with the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS–DSM-IV).
Results: Prevalence of lifetime smoking decreased across cohorts, but prevalence of ND increased among smokers. Associations between smoking and all diagnoses except MD increased in more recent cohorts (smoking × cohort interaction $p<0.05$). For DUD and AUD, increases were observed among both non-dependent and dependent smokers; for other diagnoses, they found only among ND smokers. The increasing associations remained significant when tested separately by gender.
Conclusions: More recent smokers more ND and psychiatric comorbidity, suggesting the need for regular mental-health screenings in this vulnerable cohort. Researchers should be aware of the potential confounding exerted by systematic variation in psychiatric comorbidity across different smoking cohorts, particularly if this variation has genetic underpinnings.
Financial Support: This study is funded in part by K01DA029598 from NIDA (Talati), K05AA014223 and U01AA018111 from NIAAA (Hasin), and the New York State Psychiatric Institute.

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DECISION-MAKING, IMPULSIVITY, AND DRUG SEVERITY IN CO-OCCURRING SUBSTANCE DEPENDENCE AND PATHOLOGICAL GAMBLING.

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Aims: Substance use disorder and pathological gambling share characteristics of impaired decision-making, higher impulsivity, and greater risk-taking. Having both diagnoses may be associated with greater problems than either diagnosis alone. We hypothesized that in substance dependent individuals, co-occurring pathological gambling would be associated with worse decision-making, impulsivity, risk-taking, and drug severity.
Methods: Ninety-six substance dependent individuals were recruited from a residential treatment program and divided into one of two groups depending on whether they met DSM-IV criteria for pathological gambling (SDPG, n=26) or not (SD, n=70). Ninety-two controls were recruited from the community. Subjects completed a decision-making task (modified Iowa Gambling Task), measures of impulsivity (Barratt Impulsivity Scale and Delay Discounting) and risk-taking (Balloon Analog Risk Task). Decision-making was analyzed using a computational model. We tested for group differences using ANCOVA or Kruskal-Wallis and appropriate post-hoc tests.
Results: The groups differed in decision-making computational parameters ($p<0.001$) and self-reported impulsivity ($p<0.001$). All pairwise post-hoc comparisons were significant on these measures, and indicated stepwise changes in controls, followed by SD, followed by SDPG, with SDPG performing the worst on the decision-making and being more impulsive. Compared to SD, SDPG had greater drug severity ($p<0.001$). No significant group differences were observed in delay discounting or risk-taking.
Conclusions: Pathological gambling is relatively common among substance dependent individuals in treatment. Compared to substance users without pathological gambling, patients with both disorders demonstrated worse decision-making and more drug-related problems. When evaluating patients with substance dependence, clinicians should consider assessing for pathological gambling.
Financial Support: National Institute of Drug Abuse DA024104 and DA02774

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(±)-MODAFINIL POTENTIATES COCAINE SELF-ADMINISTRATION BUT NOT THE EFFECTS ON DA LEVELS IN RODENTS.

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Aims: While the mechanisms underlying the therapeutic efficacy of (±)-Modafinil (MOD) are not fully understood, actions at the dopamine (DA) transporter (DAT) appear to be involved. With some exceptions, DAT blockers administered in combination potentiate the behavioral and reinforcing effects of psychostimulants (PSY) like cocaine (COC). That potentiation is related to increased accumbens (ACC) DA levels. However, recent clinical studies suggested efficacy of MOD in treating PSY abuse, suggesting a potential reduction of COC use in PSY abusers rather than a potentiation.
Methods: Effects of MOD and COC, were tested alone and in combination, on microdialysate ACC DA levels in rats (n=48), and mice (n=60), self-administration (SA)(n=12) in rats, and subjective effects (n=12) in mice trained to discriminate COC..
Results: MOD alone (0.03-10 mg/kg i.v.) did not maintain SA above vehicle levels when substituted for COC, but at those doses increased DA levels dose-dependently. MOD pretreatments (10-32 mg/kg i.p., 5 min prior) also dose-dependently ($p<0.05$) potentiated COC SA, but microdialysis studies showed no significant enhancement of the effects of COC (0.03-3.0 mg/kg i.v.) on stimulation of DA levels in ACC in excess of those produced by COC alone. In mice, MOD alone (10-100mg/kg) produced COC-like subjective effects and potentiated the subjective effects of low COC doses ($p<0.05$). In mice, MOD elicited significant ($p<0.05$) increases in DA levels without significant differences between ACC shell and core, distinguishing MOD from PSYs abused by humans.
Conclusions: MOD alone has a reduced PSY profile compared to COC. Our preclinical results suggest it might enhance reinforcing effects when taken in combination with sub-threshold doses of COC, independently from stimulation of DA levels. Based on clinical reports, these effects suggest a basis for use of MOD as a substitution agonist therapy for PSY abuse. Studies are in progress to better address the mechanisms underlying these effects.
Financial Support: NIDA/IRP

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CEREBROSPINAL FLUID KYNURENIC ACID AND DEPRESSIVE SYMPTOMS IN HIV-INFECTED INDIVIDUALS.

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Aims: HIV patients have higher rates of depression compared to the general population in the U.S. Although social factors and co-morbid factors (e.g., such as stimulant abuse) may contribute to the depressive symptoms, abnormalities in the kynurenic pathyway may contribute to the symptoms in HIV patients. Increased kynurenic acid (KYNA) levels were reported in cerebrospinal fluid (CSF) of HIV patients, while decreased kynurenic acid levels were reported in CSF of depressed patients. Whether KYNA concentration varies with depressive symptoms differently in those with and without HIV was explored.
Methods: 100 participants, 51 seronegative controls (SN) and 49 HIV, were evaluated clinically, provided CSF samples and completed the Center for Epidemiological Studies Depression scale (CES-D). We further evaluated the subjects according to the CESD scores (high ≥16 or low <16). CSF KYNA levels were measured by high performance liquid chromatography (HPLC).
Results: SN and HIV subjects had similar age, education and sex proportion. However, HIV subjects had higher CES-D scores. HIV subjects with high and low CES-D had similar CD4 count, nadir CD4, and viral load. Across all subjects, those with higher CES-D had lower KYNA ($p=0.025$), but HIV subjects tended to have higher levels than SN ($p=0.06$). However, HIV subjects with higher CES-D had lower [KYNA] than HIV with lower CES-D ($p=0.07$). SN with higher CES-D scores had similar [KYNA] as those with lower CES-D scores.
Conclusions: Consistent with prior studies, those with depressive symptoms had lower CSF KYNA levels. However, this is the first study to evaluate CSF [KYNA] in HIV subjects in relation to depressive symptoms. The trend for higher KYNA in HIV subjects may be related to the greater neuroinflammation. Additional evaluations with CSF and serum inflammatory markers, such as cytokines and chemokines, and other metabolites in the kynurenic pathway will be evaluated.
Financial Support: Supported by: NIH (2K24-DA16170, U54-NS56883, G12-MD007601, P30CA071789).

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CHRONIC, BUT NOT ACUTE, LOW DOSES OF PRAMIPEXOLE INCREASED RISK-TAKING BEHAVIOR IN RATS.

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Aims: Pramipexole (PPX) is a direct-acting dopamine agonist that is used to treat neurological motor disturbances, such as Parkinson's disease (PD). In a significant portion of PD patients, continuous PPX therapy is associated with behavioral addictions (e.g., pathological gambling). One aspect of gambling is increased risk-taking behavior. The aim of this study was to determine the propensity of PPX to increase risk-taking in rats using a probability discounting task wherein intracranial self-stimulation (ICSS) was used as the positive reinforcer.
Methods: The dopaminergic toxin 6-OHDA (lesioned) or its vehicle (sham) was injected bilaterally into the dorsolateral striatum of anesthetized rats. At the same time, a stimulating electrode was implanted within the lateral hypothalamus. One week later, rats were trained in an ICSS-mediated discounting task wherein they selected between a small reinforcer presented immediately after lever pressing and a large reinforcer presented after varying probabilities. After stable behavior was observed (<20% variability for three consecutive sessions), an osmotic mini-pump was inserted subcutaneously, to deliver 0.3mg/kg/day PPX for 14 days. The discounting task was tested daily.
Results: Lesioned and sham rats acquired the task equally and there was no difference between baseline discounting. Acute PPX (i.e., day 1 following mini-pump implant) had no effect on risk-taking behavior in either group. In contrast, chronic treatment with 0.3mg/kg/day PPX increased risk-taking behavior in both groups. All rats returned to baseline levels ~1week after the PPX mini-pump was removed.
Conclusions: These data reveal that a PPX dose which is subthreshold to altering behaviors when given acutely, was sufficient to increased risk-taking in a probability discounting task in both sham control and lesioned rats following chronic treatment. These findings also support the idea that behavioral addictions can be induced by PPX independent of PD neuropathology.
Financial Support: USPHSGs #NS074014 and #DA033121.

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THE ROLE OF SELF-EFFICACY IN PREDICTING PERINATAL WOMEN'S ABILITY TO REDUCE SMOKING.

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Aims: Smoking during pregnancy/postpartum has been associated with a host of negative outcomes for mother and child. An increased understanding of factors related to pregnant women's decision and ability to quit smoking would inform the development of intervention programs. Thus, the purpose of the current exploratory study is to determine whether pregnant smokers who believe in their ability to quit/reduce smoking (high self-efficacy) are more successful than their counterparts low in self-efficacy.
Methods: Data for the current exploratory study (n=28) consist of the first 3 visits of a double-blind placebo-controlled clinical trial examining the use of Bupropion as a smoking cessation aid during pregnancy. Visit 1 included enrollment and drug dispensation (active or placebo) and visit 2 was the "quit day." At each visit, patients self-reported the number of cigarettes smoked per day. Smoking self-efficacy (SE) was assessed on the first visit with a 9-item scale adapted from a larger SE scale.
Results: A summary score was calculated for each participant and high and low SE groups were created. The low SE group consisted of the bottom third percentile and the high SE group consisted of the remaining. A profile plot identified the trend of cigarette frequency over the three clinic visits for both the high and low SE groups. Essentially, women in both groups evidenced similar reductions in cigarettes per day by their third visit (from 12 cigarettes at baseline to 4). However, relative to those low in smoking SE, women high in smoking SE were able to reduce their smoking more quickly, as evidenced by steeper reductions in cigarettes smoked per day as reported at visit 2.
Conclusions: While preliminary, findings indicate that motivational interviewing or other techniques aimed at increasing women's self-efficacy in their ability to quit smoking may expedite their decision and ability to quit smoking.
Financial Support: Supported by a NIDA grant RO1DA030998 to TN and GH

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HOW WELL DO WE UNDERSTAND OLDER FEMALE SUBSTANCE ABUSERS IN THE U.S.? AN ANALYSIS OF TEDS-D 2006-09.

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Aims: Historically, substance abuse (SA) has been considered a problem of young people, especially men. Hence less is known about the nature of SA in older women. The number of baby boomers in the US suggests that as this cohort ages, there will be an increased need for services specific to older women.
Methods: Data were drawn from the Treatment Episode Data Set – Discharges (TEDS-D). Analysis compared women under 50 (n=1,878,067) to those 50 and over (N=182,246) via multivariable logistic regression. Characteristics included were race/ethnicity, education, source of income, living arrangements, primary substance, age at first use, days awaiting treatment, referral source, number of substances, treatment setting, and prior episodes.
Results: In demographic comparisons, older women were more likely to be black (OR=2.57 [2.52, 2.66]), divorced/widowed (OR=1.39 [1.35,1.42]), high school graduates (OR=1.43 [1.39, 1.47]), homeless (OR=1.32 [1.25, 1.34]), receiving retirement or disability income (OR=3.40 [3.29, 3.51]), and to have started use of their primary drug as adults (OR 2.21 [2.17, 2.27]). Older women were also more likely to have prior treatment episodes and be enrolled for alcohol, which may explain many of the treatment characteristics observed. Specifically, older women were more likely than younger women to go into detoxification and have short wait times, and less likely to have criminal justice referrals (OR=0.87 [0.84, 0.88]).
Conclusions: These findings suggest there are differences between older and younger women in treatment. These may be the result of cohort effects or evidence of changes in SA as women age. There is need to further investigate the factors driving these differences to better inform healthcare policies and treatment services for this population.
Financial Support: None

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PHYSICAL DEPENDENCE LIABILITY OF RETIGABINE IN RATS.

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Aims: Retigabine (RTG) is an antiepileptic drug with a novel mechanism of action acting through the potentiation of KCNQ2/3 potassium channel, which are important in controlling neuronal excitability. In vitro evidence additionally suggests RTG augments GABA-mediated neurotransmission which may contribute a stabilizing effect on neuronal excitability. A key component in non-clinical abuse liability testing is the evaluation of a potential withdrawal syndrome induced by chronic administration, and abrupt cessation, of the test article. The objective of this study was to assess the potential of RTG to induce a withdrawal syndrome following abrupt cessation during chronic administration in Sprague Dawley rats.
Methods: Rats were orally treated with 3, 10 and 30 mg/kg/day RTG for 28 days and then observed for 14 days following the cessation of RTG treatment. Chlordiazepoxide HCl (CDP) was selected as the positive control. CDP was administered in incremental doses: 20 mg/kg on Day 1, 40 mg/kg on Day 2 and successive increments of 20 mg/kg each day until the dose of 200 mg/kg was reached. This dose was then maintained to Day 28.
Results: Following RTG cessation, no changes in body weight, food consumption or body temperature were observed and only some animals showed minor behavioural effects. Discontinuation of RTG after repeated administration induced a behavioural profile distinctly different from that observed following discontinuation of CDP.
Conclusions: Whereas robust physiological and behavioural withdrawal symptoms were observed in the CDP-treated animals similar to that documented in the literature for benzodiazepines, the RTG-treated groups showed no withdrawal effects on physiological parameters and only a mild, non dose-dependent increase in behavioural parameters. Based on these findings, chronic administration of RTG in rats did not result in a withdrawal syndrome following abrupt discontinuation.
Financial Support: Authors did not received any financial support

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EMERGING ADULT GENDER DIFFERENCES IN SEXUAL DISCOUNTING AND HIV RISK BEHAVIOR.

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Aims: Sexual risk behavior is a leading cause of death and disability in emerging adults (EA). Individuals ages 15-24 account for 50% of all new STIs and is the only age group to experience a rise in the rate of HIV infection. Women face serious health consequences as a result of STIs. EA may be highly insensitive to the delayed consequences of sexual risk taking and exhibit preferences for immediate gratification. The present abstract aims to examine sexual discounting (SD) and HIV-related behaviors in a sample of EA.
Methods: We examined SD and patterns of HIV risk using ANOVA and regression. Participants consisted of 100 EA (female = 66%, Mage = 20.39).
Results: Analyses revealed gender differences in SD ($F(2,98) = 7.49$; $p < 0.01$), with males more likely to discount a delayed sexual commodity. SD was predictive ($\alpha = 0.05$) of lifetime partners for males [(oral sex: B = -0.514); (vaginal sex = -0.319)] but not females. Although SD was predictive of having unprotected vaginal sex (B = 0.420) and frequency of condom use during vaginal sex for males (B = 0.398); for females it was predictive of having unprotected vaginal sex (B = 0.292), frequency of condom use [(oral sex: B = 0.253); (vaginal sex: B = 0.406)], as well as approaching significance for having unprotected anal sex (B = 0.179) and frequency of condom use during anal sex (B = 0.062). Regarding casual sex practices, SD was related to engaging in vaginal sex with a recently met partner (B = 0.325), a non-committed partner (0.344), and multiple partners (B = 0.297), as well as with multiple oral sex partners (B = 0.226) for males. For females it was related to engaging in oral sex with a recently met partner (B = 0.201) and non-committed partner (B = 0.238), as well as engaging in vaginal intercourse with multiple partners (B = 0.278), and approaching significance for engaging in vaginal sex with a non-committed partner (B = 0.152).
Conclusions: Sexual discounting, which manifests differently among sexes, is a critical variable for understanding HIV risk behavior and may explain HIV vulnerability in EA, especially in young females.
Financial Support: TAMU Vision 2020 Dissertation Enhancement Award

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DEVELOPMENT OF A WORKFLOW FOR SCREENING FOR THE HEPATITIS C VIRUS IN HIV-POSITIVE IV DRUG USERS.

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Aims: HCV infection is the most common blood-borne infection in the US that is spread through IV drug use. Recent data has demonstrated that IV drug users can act as "super-spreaders" of HCV as they are likely to infect approximately 20 other individuals with most transmissions occurring in the first two years after their initial infection.
Methods: This commentary assess methodologies to identify HCV infected IV drug users
Results: Based on evaluation of current HCV screening methodologies, the new rapid point-of-care (POC) HCV antibody test would be the best methodology to perform initial screening for HCV. The cost of the POC test would be <$20 per persons. All patients that are antibody positive would then be subject to venipuncture for diagnostic testing for confirmation of active infection and quantitation of HCV RNA levels. The cost of the diagnostic test for HCV RNA quantitation would be approximately $130 per person. In the patients that are HCV RNA positive, HCV Genotyping will then be performed. The cost of the genotyping diagnostic test would be approximately $150 per person. After genotyping, the patients are then ready for linkage to care for consideration for HCV antiviral therapy with the new antiviral agents. Thus, an individual can be completely screened and be ready for medical evaluation for $300. Of the tests mentioned, the only one that is amenable for high throughput analyses is HCV RNA quantitation. Consequently, the POC test will be the limiting factor of the number of individuals that are able to be screened and also will comprise the greatest cost.
Conclusions: A new rapid point-of-care test is now available to diagnose patients with HCV. Furthermore, very potent antiviral agents are expected to gain FDA approval within the next 3 years. Consequently, a unique opportunity now exists to minimize poor clinical outcomes resulting from HCV, which spreads through IV drug use.
Financial Support: University of Miami Schiff Center for Liver Diseases and NIDA R25DA030310 (PI Jim Anthony)

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CHRONIC TREATMENT WITH THE MONOAMINE RELEASER PHENMETRAZINE REDUCES COCAINE SELF-ADMINISTRATION AND COCAINE-INDUCED REINSTATEMENT.

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Aims: Despite limited success, there are still no FDA-approved medications for cocaine addiction. Monoamine releasers have shown promise in clinical and preclinical studies. Phenmetrazine (PM) also releases monoamines and its prodrug phendimetrazine has very low abuse liability. The aims of the current study were to determine whether PM reduces cocaine self-administration (SA) and cocaine-primed reinstatement.

Methods: Rats were trained to self-administer cocaine on a fixed-ratio (FR) 1 schedule (0.75 mg/kg/inf). In experiment one, rats were switched to a progressive ratio (PR) schedule (0.19 mg/kg/inf). After stable PR performance, rats were implanted with subcutaneous osmotic minipumps delivering either vehicle (n=8) or PM (25 or 50 mg/kg/day, n=8 per group). Rats continued on the PR schedule for 14 days, and then the effect of discontinuation of PM treatment on break points was investigated for 7 days. In experiment two, rats (n=8 per group) were switched to long-access conditions (0.75 mg/kg/inf, FR1, 6h sessions) for 14 days, followed by implantation of subcutaneous osmotic minipumps delivering vehicle, amphetamine (5 mg/kg/day) or phenmetrazine (50 mg/kg/day). Seven days later, rats began daily 2h extinction sessions which lasted at least 7 days and until extinction criteria were reached (≤ 25% of mean number of responses of the last two days of SA). The priming effect of cocaine (10 mg/kg, i.p.) on lever responding was then determined.

Results: Phenmetrazine significantly reduced break points ($P < 0.01$), which remained lower than controls during the 7 day washout period. The cocaine prime significantly reinstated responding in animals implanted with saline minipumps ($P < 0.01$), but failed to reinstate responding in animals receiving chronic amphetamine or phenmetrazine.

Conclusions: These data extend previous studies with amphetamine, and indicate that chronic treatment with monoamine releasers, such as phenmetrazine, may significantly mitigate the reinforcing effects of cocaine.

Financial Support: NIDA P50 DA06634

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COMPARISON OF PERCEPTIONS OF HIV RISK AND RISKY SEXUAL PRACTICES AMONG HETEROSEXUAL COCAINE-DEPENDENT INDIVIDUALS.

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Aims: Cocaine use is associated with higher prevalence of risky sexual behavior, ultimately leading to a greater risk of sexually transmitted diseases. Our ongoing study compares the perception of risk of HIV and attitudes towards condom use with actual sexual practices in heterosexual cocaine dependent (CD) individuals and non-drug using controls.

Methods: To date 23 CD individuals and 18 controls have been recruited. Self-report measures of attitudes towards sexual behaviors and perceptions of risk were measured via Sexual Risks Scale-Attitudes Towards Condom Use (SRSA), Limiting HIV Risk Behavior (LHRB), Risk Behavior Assessment (RBA), Perceived Risk HIV and Risky Sex Scale (RSS).

Results: CD participants reported having sex 7.6±1.5 (Mean±S.E.M.) days out of the last 30 whereas controls reported having sex 4.0±1.4 days of the last 30 ($p=0.11$). Also, CD participants reported having 1.6±1.0 sexual partners while controls reported having 1.0±0.0 sexual partners in the last 30 days ($p=0.086$). CD participants had more negative attitudes towards condom use as determined by the SRSA ($p=0.047$). There were no significant differences between CD participants and controls with respect to perception of risk following unprotected and protected oral, vaginal, and anal sex regardless of HIV status (all p's >0.05), with the exception of HIV negative status where CD participants (18.7±4.9) associated more risk of HIV than control participants (5.6±3.1) during unprotected vaginal sex ($p=0.05$).

Conclusions: Despite minimal differences in perception of risk of HIV between groups, heterosexual CD participants are more likely to engage in more sex acts with more partners than matched controls. Additional data for this project includes evaluations of neural responses during a sexual discounting task.

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LOSS OF SELF-CONTROL OVER DRINKING AND THE RELATIONSHIP OF ALEXITHYMIA TO QUALITY OF LIFE IN ALCOHOL-DEPENDENT PATIENTS.

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Aims: Up to 67% of alcohol-dependent patients in treatment have alexithymia, a personality trait associated with emotion regulation difficulties. Alexithymia has been investigated in relation to quality of life (QoL) among male alcohol-dependent patients, but no study has explored gender differences or underlying mechanisms that link alexithymia with QoL. The objective of the present study, therefore, was to address these questions and to examine the extent to which obsessive thoughts about alcohol use and compulsive behaviors mediate the relationship between alexithymia and QoL.

Methods: 396 patients 18-71 years of age, undertaking outpatient Cognitive-Behavioural Therapy for alcohol dependence were recruited. Participants were detoxified prior to assessment, and completed the Toronto Alexithymia Scale (TAS-20), the Obsessive Compulsive Drinking Scale (OCDS) and the Health Survey (SF-36).

Results: TAS-20 total score, Difficulties Identifying Feelings (DIF) and Difficulties Describing Feelings (DDF) were more strongly correlated with parameters of QoL for males than for female participants. Path analyses showed that for males OCDS scores fully mediated the relationship of DIF with physical QoL and partially mediated the relationship with emotional QoL. For females OCDS scores partially mediated the relationships of DIF with emotional as well as physical QoL.

Conclusions: Loss of control over drinking appears to be a mediator of the link between alexithymia and QoL, and the neural circuitry that mediates self control may be a treatment target in alcohol-dependent treatment seekers with alexithymia.

Financial Support: Innlandet Hospital Trust.

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MOBILE PHONE AND TEXT MESSAGING IN A PUBLIC SECTOR, OFFICE-BASED BUPRENORPHINE PROGRAM.

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Aims: We conducted a descriptive, cross-sectional survey exploring mobile phone and TM use patterns and preferences pertaining to their substance treatment in a public sector, office-based buprenorphine program.

Methods: A 28-item, quantitative and qualitative semi-structured survey was administered to 71 patients enrolled in a public sector, office-based buprenorphine program between June and September 2013. Survey domains included: demographic characteristics, mobile phone and TM use patterns, and mobile phone and TM use patterns and preferences pertaining to their substance treatment.

Results: Mobile phone ownership was common (93%) with no significant differences in ownership among self-reported homeless, recently incarcerated, and unemployed respondents. Most reported sending or receiving TM (93%) and reporting 'very much' or 'somewhat' comfort sending TM (79%). Contacting buprenorphine providers by phone (30%) or TM (17%) was uncommon, however most preferred to use either form of communication to reach their provider (67%). Older patients received less TM (25) compared to younger age groups (128) yet were as interested as the rest of the clinic population to have their provider's mobile phone number (96%) and send TM if at risk of relapse (78%).

Conclusions: Our findings highlight the acceptability of enhancing patient-provider mobile phone and TM communications in a public sector, office-based buprenorphine clinic, even among respondents that were not comfortable in using TM. Although mobile phone ownership was very common, frequent turnover in phone ownership and changing phone numbers highlights challenges in feasibility for any future mhealth interventions in this clinical setting.

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WHAT IS THE MOST COST-EFFECTIVE ADVERTISING STRATEGY FOR ALCOHOL PHARMACOTHERAPY CLINICAL TRIALS?

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Aims: Randomized controlled trials (RCTs) for alcohol use disorder (AUD) pharmacotherapies can be hampered by ineffective recruitment, leading to increased trial costs or underpowered studies. The current analyses examined the recruitment effectiveness of different advertising mechanisms during two consecutive outpatient RCTs of novel AUD pharmacotherapies.
Methods: Trials were conducted during 2009-2012. During an initial phone screen, participants identified one of eight ad sources for learning about the study. Qualified persons were then scheduled for an in-person screen. Recruitment effectiveness was defined as the proportion of persons meeting criteria for an in-person screen for each ad source. Cost-effectiveness was determined by dividing the total cost for each ad source by the respective number of phone screens, in-person screens, participants randomized, and completers it produced. Differences between ad sources were examined using chi square tests.
Results: 1,813 calls resulted in 1,005 completed phone screens. The most common ad source given by callers was TV (34%), followed by print (29%), word-of-mouth (11%), flyer (8%), internet (5%), radio (5%), bus ad (2%), and billboard (1%). There was a significant difference between ad sources in the percentage of qualified callers scheduled for an in-person screen [$\chi 2(8, N=1005)=23.9$, $p=0.002$]. Participants reporting bus ads (46%), billboard (44%), or print ads (34%) were significantly more likely than the other sources to be scheduled for an in-person screen. The most cost-effective ad source was print ($2,506 per completer), while billboard was the least cost-effective ($13,376 per completer).
Conclusions: Recruitment in AUD RCTs can be successful using diverse advertising methods. The present analyses favored use of print ads as the most cost-effective approach for these trials.
Financial Support: This work was funded by NIDA (5T32 DA07209, K24 DA023186, K23 DA029609) as well as two subcontracts from NIAAA administered by Fast-Track Drugs and Biologics, LLC.

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DELAY DISCOUNTING PREDICTS PREFERENCE REVERSALS BY CIGARETTE SMOKERS.

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Aims: Preference reversals (PR) in intertemporal choice, predicted by delay discounting (DD) models, are thought to model self-control failures such as smoking relapse. No research has explicitly attempted to predict PRs from DD rates. The present research evaluates this relationship with cigarette smokers.
Methods: Thirty-one (31) cigarette smokers met at least two of the following: 1) DSM-IV nicotine dependence, 2) Score ≥5 on the FTQ, 3) Self-report smoking ≥ 20 cigarettes/day, 1 year minimum. Participants completed a novel 86-item binary choice measure with 27 now-vs-later items (Monetary Choice Questionnaire), and 59 later-vs-later items. Hyperbolic DD rates *(k)* were determined for three magnitudes using the now-vs-later items, and *Observed* PRs *(OPR)* were determined using the later-vs-later items.
Results: *Predicted* PRs *(PPR)* were determined for each corresponding *OPR* using individual DD rates. Linear regression (y-intercept=0) with *PPR* (predictor variable) and *OPR* (outcome variable) was conducted. A slope (*b*) of 1 indicates unbiased correspondence between *PPR* and *OPR*. The mean slope across magnitudes was .96 (*SE*=.03). *PPR* based on hyperbolic discounting were classified "excellent" (10% of *b*=1) for 80.6% of participants and classified "good" (20% of *b*=1) for 87.1% of participants across all magnitudes.
Conclusions: Hyperbolic DD rates appear to predict PRs. These results advance hyperbolic discounting as a construct relevant with self-control failures and their timing. This research provides proof of concept that indices of a cigarette smoker's valuation of future outcomes (*k*) may help predict smoking relapse timing (modeled by PRs). Knowledge of relapse vulnerability timing could be used for temporally targeted interventions to promote abstinence.
Financial Support: National Institute on Drug Abuse

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ACUTE STRESS RESPONSE IN COCAINE-DEPENDENT SUBJECTS WITH COMORBID DEPRESSION.

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Aims: To evaluate some components of the acute stress response in cocaine dependent patients with independent or substance-induced major depression.
Methods: A total of 23 cocaine dependent patients (DSM-IV-TR) (14 with comorbid independent major depression and 9 with comorbid cocaine-induced major depression) and 20 healthy controls. To evaluate acute stress response the Trier Social Stress Test (TSST) was used. Plasma cortisol levels and anxiety scores (using STAI-S) were measured before TSST (pre-TSST), immediately after TSST (post-TSST) and 30 minutes later (post-30'TSST). The data were analyzed with repeated measures ANOVA and post hoc analysis using the Bonferroni test.
Results: In cocaine dependent subjects, those with independent depression showed a stress response similar to controls, but cocaine-induced depression subjects did not present reactivity to stress, in both, cortisol levels and STAI scores.
Conclusions: These preliminary results show a different response to acute stress between patients with independent or cocaine-induced major depression. Stress response could be a biomarker to differentiate depression in cocaine dependent subjects.
Financial Support: Founded in part by grants from by FIS (PS09/02121), Red de TrastornosAdictivos (RD06/0001/1009) and ISCIII-Rio Hortega contract (CM12/00085).

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MTOR-DEPENDENT PLASTICITY: DON'T FORGET MACROAUTOPHAGY.

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Aims: Given the recently-elucidated role of macroautophagy in synaptic plasticity, we decided to explore its potential implications in mediating the effects of drugs of abuse. Gradually, the molecular mechanisms underlying MSNs gaining more spines in response to psychostimulants, are being elucidated. However, what is known, stems from studies using cocaine, and not amphetamine. In order to begin to both draw parallels and establish distinctions between the means employed to increase spine density, we explored the possible role of proteins residing in the spine, specifically the postsynaptic density scaffold protein PSD95.
Methods: We generated D1R-specific macroautophagy conditional knockouts and investigated whether different types of striatal postsynaptic properties are dependent on the presence of this process, namely PSD size and number. Before characterizing the role of mTOR and macroautophagy in psychostimulant-induced plasticity, we began by assessing how an acute injection of amphetamine at multiple doses and times of collection after treatment influences striatal PSD95 by western blotting.
Results: We found that amphetamine failed to robustly modify levels of PSD95 in striatal homogenates. However, we found that, basally, our macroautophagy-deficient mice have significantly larger postsynaptic densities in the striatum.
Conclusions: Our data raises several points, including the possibility that unlike cocaine, acute or short regimens of amphetamine might not regulate spine density in the striatum. It underscores the importance of the fact that despite similarities between these drugs, while it might be tempting to extrapolate, it is crucial to examine their effects separately. Finally, it provides a starting point to undertake the study of how acute amphetamine affects molecular, morphological, functional and whole animal behavior.
Financial Support: Currently supported by NIDA07418.

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EFFECTS OF HIV INFECTION AND COCAINE DEPENDENCE ON NEUROCOGNITIVE IMPAIRMENT.

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Aims: Drug dependence and HIV infection are both brain diseases that can cause neurocognitive impairment, but few studies have empirically tested whether co-occurring HIV infection and stimulant abuse have compounding effects on neurocognitive functioning. The purpose of this study is to investigate the effects of HIV infection and cocaine dependence on neurocognitive impairment
Methods: To date, the sample includes 152 adult participants across four groups who differed on cocaine dependence and HIV status: HIV-positive cocaine users (n= 44), HIV-negative cocaine users (n= 46), HIV-positive non-drug users (n= 51), and HIV-negative non-drug users (n= 11). Cocaine use was verified by urine drug screen and clinical interviews, including the Addiction Severity Index and the Structured Clinical Interview for the DSM-IV. HIV-status was confirmed using a rapid test for HIV-negative participants and medical record review for HIV-positive participants. A comprehensive battery was used to assess neurocognitive functioning. Trained psychometrists administered and scored the neuropsychological tests. Global Deficit Scores were computed by averaging standardized T scores across seven domains.
Results: The sample is mostly male (66%) and African American (86%), with a mean age of 45 years. Cocaine users had used cocaine 10.5 days on average in the past month. HIV-infected participants had been diagnosed with HIV for 12.8 years on average. There was a significant main effect of cocaine ($p = .013$), such that cocaine users had lower average T scores than non-users, but there was no main effect for HIV ($p = 0.462$), and no significant interaction of cocaine and HIV ($p = 0.556$). This pattern of effects was similar across each domain when examined individually.
Conclusions: As expected, cocaine users demonstrated poorer performance on testing than non-users. Contrary to hypothesis, we did not see a main effect for HIV or an interaction effect. Additional analyses will examine the potential moderating role of markers of HIV disease progression.
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PREDICTORS OF SUBSTANCE USE OUTCOMES IN MENTORSHIP FOR ADDICTION PROBLEMS.

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Aims: We conducted a Stage Ia pilot to develop a new intervention, Mentorship for Addiction Problems (MAP), for individuals with substance use disorders in community treatment programs by pilot/feasibility testing, manual writing, training program development, and adherence/competence measure construction. We examined intervention and participant predictors of substance use outcomes.
Methods: Ten Mentors participated for 6 months in a piloting of MAP until 30 Mentees received MAP for 12 weeks. Behavioral and biological measures were conducted at baseline, weekly, monthly, and termination. A series of bivariate regressions were conducted to determine whether any treatment process or participant variables were associated with substance use outcomes.
Results: Intervention Predictors. Mentor group supervision attendance was predictive of Mentee percentage of days abstinent from drugs and alcohol for Mentee weeks in treatment, $R2=.790$, $F(1, 8)=30.13$, $p<.001$, and predictive of Mentee percentage of days abstinent from drugs $R2=.458$, $F(1, 8)=6.76$, $p<.05$. Mentee overall attendance was predictive of percentage of days of Mentee abstinence from alcohol, $R2=.158$, $F(1, 28)=5.27$, $p<.05$ and percentage of days of Mentee abstinence from drugs and alcohol, $R2=.228$, $F(1, 28)=8.28$, $p<.05$. Finally, Mentor overall attendance was predictive of Mentee percentage of days abstinent from drugs, $R2 =.462$, $F(1, 8) =6.86$, $p<.05$, and predictive of Mentee percentage of days abstinent from drugs and alcohol $R2=.798$, $F(1, 8)=31.50$, $p<.001$. Participant Predictors. Similar analyses did not find any demographic, housing stability, substance abuse severity or prior substance and psychiatric treatment variables to be associated with outcome.
Conclusions: MAP treatment process variables were associated with substance use outcomes.
Financial Support: We would like to thank NIAAA and NIDA for their support of this work through the following grants R01AA016160 and R34DA034898.

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HEPATITIS C VIRUS INFECTION, HIV AND PAIN SENSITIVITY IN OPIOID-DEPENDENT PATIENTS.

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Aims: Opioid dependent patients on opioid agonist treatment (OAT) have lower tolerance to experimental pain compared to non-opioid dependent controls. Some observational studies suggest that patients with hepatitis C virus (HCV) may be at risk for pain. No studies have examined whether HCV may contribute to pain sensitivity in this population.
Methods: Cross-sectional study of opioid dependent adults on OAT (buprenorphine or methadone) to explore whether HCV-infected had greater experimental pain sensitivity and self-reported pain. The primary outcome was cold pain tolerance (cold-pressor test). Secondary outcomes were standard pain measures: 1) cold pain thresholds 2) temporal summation (wind-up ratio to repetitive pinprick) and 3) self-reported chronic pain (>3 months). The independent variable was HCV status (uninfected controls; mono-infected HCV+; or co-infected HCV+/HIV+). Chi-square and Kruskal-Willis tests were conducted.
Results: The sample included 77 opioid-dependent adults: 23 uninfected controls, 35 HCV+, and 19 HCV+/HIV+. Mean age was 44 (SD±9) years, 48% were female, 32% non-white. Median duration on OAT was 2 years (range 1 month to 10 years), the majority (83%) were treated with buprenorphine. No significant differences were detected across groups for both primary and secondary outcomes. Median cold pain tolerance was 22 (controls) vs. 30 (HCV+) vs. 19 (HCV+/HIV+) seconds, ($p=0.63$). No significant effects were found for cold pain thresholds or wind-up ratio. Chronic pain appeared more prevalent among HCV+ (82%) compared to HCV+/HIV+ participants (63%) and controls (65%), though differences were not statistically significant ($p=0.21$).
Conclusions: Among opioid dependent adults treated with OAT, we did not detect an association between HCV infection and increased pain sensitivity. Chronic pain may be more common among HCV mono-infected individuals, however this merits further investigation.
Financial Support: This study is supported by NIH/NIDA grant K23DA027367.

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WHO IN THE WORLD BUYS ARVS ON THE BLACK MARKET? THE IMPACT OF DRUG USE AND ARV DIVERSION ON ADHERENCE.

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Aims: Anti-retroviral (ARV) adherence is the most important predictor of regimen success and HIV viral suppression. HIV-positive drug users are found to have less access to ARV treatment and to initiate treatment at more advanced stages of infection than non-drug users. Recent studies also identify ARV diversion as a factor that may affect ARV adherence in drug users. This study examines motivations behind buying ARVs on the black market with a focus on the role of drug use and ARV diversion on ARV adherence.
Methods: Semi-structured, in-depth interviews were conducted with 44 people living with HIV who reported purchasing ARVs on the street at least once in the past three months. Respondents gave detailed information about their drug use, ARV adherence, and history of buying ARVs on the street. Grounded theory was used to code and analyze interviews using Atlas.ti.
Results: The sample averaged 46 years old (SD=7.8), 59% male, and 43% non-Hispanic Black. 36% of participants reported drinking alcohol, 34% used crack, 27% used cocaine, 23% used marijuana, and 9% used heroin. Motivations for buying ARVs on the black market included: having sold or lost ARVs, having provider or insurance-related barriers to the legal access of ARVs, and profit-making. The most common motivation for buying ARVs illicitly was to replace a legitimately obtained prescription that was sold for money to purchase illicit drugs, personal items, or to pay bills. The data suggest that drug dependence undermines ARV adherence in several ways. Participants mentioned that drug seeking and use impeded ARV adherence and the desire not to mix illicit drugs and ARVs in their system.
Conclusions: Limited ARV adherence among substance users may further exacerbate the risk of treatment failure, ARV resistance, and HIV transmission. Our study highlights a need for HIV literacy education, accessible drug treatment programs, and interventions to support ARV adherence.
Financial Support: This research is supported by NIDA grant R01DA023157.

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THE ASSOCIATION BETWEEN EXPOSURE TO GUNS AND GAMBLING AMONG COMMUNITY-RECRUITED SUBSTANCE USING WOMEN.

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Aims: These analyses examine the association between exposure to guns and gambling among 838 alcohol and drug using women in St Louis.
Methods: Women were recruited from two community based HIV prevention intervention studies (NIAAA-Sister-to-Sister, and NIDA-Women Teaching Women); the Diagnostic Interview Schedule (DIS) obtained information on DSM-IV pathological gambling (PG) and the Violence Exposure Questionnaire (VEQ) assessed access to a gun, gun ownership and gun carrying.
Results: Women were predominantly African American (80%) with a mean age of 35.7 years (± 8.8); 505 (60%) never owned, had access to or carried a gun, 145 (17%) had immediate access to a gun and 188 (22%) had a history of carrying a gun. Five typologies of gambling behavior were identified – never gambled (n=232, 28%); gambled <5 times in a year with no PG criteria (n=281, 33%); gambled at least 5 times with no PG criteria (n=145, 17%); gambled at least 5 times with 1-4 PG criteria met (n=128, 15%); and gambled at least 5 times and met 5+ PG criteria (n=52, 6%). As the frequency of gambling and PG increased, access to guns increased – 13% of never gambled, 17% of gambled <5 times with no PG criteria, 29% of gambled at least 5 times with no PG criteria, 35% of gambled 5+ times with 1-4 PG criteria and 44% of gambled 5+ times and met 5+ PG criteria, had access to a gun (p<. 0001). Likewise, gun carrying increased across the five typologies of gambling (22% vs. 28% vs. 36% vs. 46% vs. 46%, p<. 0001).
Conclusions: The findings indicate that substance using women with gambling problems have higher odds for exposure to guns indicating a need for screening and interventions to reduce these public health risks.
Financial Support: NIAAA # AA12111, Cottler, PI and NIDA # DA11622, Cottler, PI.

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FEASIBILITY OF THE QUIT USING DRUGS INTERVENTION TRIAL.

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Aims: Early detection and treatment of casual or regular drug use in primary care settings can be a feasible and effective way to intervene and interrupt progression to drug dependence. We report on the feasibility of conducting the UCLA Quit Using Drugs Intervention Trial (QUIT), a brief intervention for reducing risky drug use, progression to dependence, and drug-related harm in low-income, racially diverse patients of 5 Federally Qualified Health Centers (FQHCs) in Los Angeles.
Methods: All adult patients in 5 FQHC waiting rooms were screened using a self-administered version of the WHO ASSIST on a touch-screen Tablet PC. Eligible risky drug users (ASSIST score 4-26) were randomized to the QUIT intervention (n=171). We report on measures of feasibility of the 4 components of the QUIT intervention: 1) brief clinician advice regarding the importance of changing drug use; 2) a brief educational video of standardized clinician advice; 3) drug-use educational booklet; and 4) 2 telephone drug-use health education (HE) sessions. Data were obtained from patients' 3-month follow-up survey, clinicians' post-study survey, and educators' HE session progress notes.
Results: 1) Of the intervention patients, 100% received the brief clinician advice, 2/3s of which took 3-4 minutes or less. 2) 90% viewed the video. 3) 100% received the drug use booklet; 4) 77% patients received the 2-week HE session, and 54% received the 6-week HE session. The average HE session lasted about 19 minutes. 68% found the brief clinician advice helpful in reducing their drug use. 85% of patients found the HE sessions to be useful in reducing their drug use (40% wanted more than 2 sessions).
Conclusions: Findings on the ease of providing the QUIT intervention and patient satisfaction with the intervention support QUIT as a feasible model for screening and intervening on risky drug use in FQHCs. Implementing QUIT as a part of routine care in primary care clinics would be an effective part of integrating behavioral health into comprehensive, patient-centered primary care.
Financial Support: NIDA DA 022445

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PREDISPOSING GENETIC DIFFERENCES CONTRIBUTE TO VULNERABILITY TO ESCALATE COCAINE INTAKE IN RATS.

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Aims: Endogenous opioids play a central role in mediating the reinforcing properties of cocaine. The striatum is a key brain region implicated in reward and motivation. Recently we published a new model of cocaine self-administration in which rats are exposed to operant sessions lasting 18h for 14 days, which models closely the human cocaine exposure (Picetti R. et al., 2010). Indeed we reported Lewis rats escalated progressively their cocaine consumption while Fischer did not. Therefore, the aim of this study was to investigate if differences in striatal endogenous opioids could contribute to the vulnerability to escalate cocaine intake.
Methods: Adult male Fischer and Lewis rats were trained to self-administer cocaine intravenously. Saline-yoked rats were used as control. Rats were sacrificed 24 h following the last operant session. Striatal cDNA samples (n= 10-11/group) were analyzed by qPCR targeting endogenous opioid peptides and receptors.
Results: POMC mRNA expression was lowered significantly by cocaine self-administration in the dorsal striatum of both Fischer and Lewis rats. Further, POMC basal level was significantly lower in Fischer than in Lewis rats. Striatal pDyn gene expression was increased by chronic cocaine in both strains; the increase seen in Lewis was much greater than in Fischer. The basal levels of pDyn mRNA was higher in Fischer than in Lewis rats. Finally, Fischer rats showed a higher basal level of mu opioid receptor mRNA than Lewis rats. Extended cocaine self-administration increased the mu opioid receptor mRNA only in Lewis, but not Fischer rats.
Conclusions: The present results corroborate the hypothesis that predisposing genetic factors could contribute to the escalation of intake in rodent models of cocaine addiction. High basal striatal pDyn could countermodulate the cocaine-induced increase in mu receptor, and decrease the progression from impulsive to compulsive drug use.
Financial Support: The Dorothea Dix Fellowship Fund (MV), NIDA P50/05130 (MJK), The Adelson Medical Research Foundation (MJK).

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NALTREXONE INHIBITS THE SUBJECTIVE EFFECTS OF SALVINORIN-A IN HUMANS.

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Aims: Salvinorin-A is a terpene found in the leaves of the plant Salvia divinorum. When administered to humans, salvinorin-A induces an intense but short-lasting modified state of awareness, sharing features with those induced by the serotonergic psychedelics. However, unlike substances such as psilocybin, or mescaline, salvinorin-A shows affinity in vitro for the kappa-opioid receptor rather than for the serotonin-2A receptor. In the present study we aimed to assess whether the subjective effects induced by salvinorin-A in humans are caused by the drug's interaction with opioid receptors.
Methods: Eight healthy volunteers participated in four experimental sessions. They received the following drug combinations one week apart: placebo/placebo, placebo/salvinorin-A, naltrexone/placebo and naltrexone/salvinorin-A. Naltrexone was administered at a dose of 50mg orally and salvinorin-A at 1mg vaporized. Subjective effects were assessed using visual analog scales (VAS), the Hallucinogen Rating Scale (HRS), the Addiction Research Center Inventory (ARCI) and the Altered States of Consciousness questionnaire (APZ).
Results: After the placebo pre-treatment, salvinorin-A induced an intense dream-like state characterized by significant increases in VAS measuring modifications in body perception, perception of time, detachment from external reality and visual imagery. Significant increases were also observed in all subscales of the HRS and APZ and in the LSD subscale of the ARCI. These effects were effectively prevented by naltrexone. Following pre-treatment with this non-specific opioid antagonist, the intensity of subjective effects induced by salvinorin-A was markedly attenuated and scores on the administered instruments were significantly decreased.
Conclusions: These results support opioid receptor agonism as the mechanism of action underlying the subjective effects of salvinorin-A in humans.
Financial Support: Grant PI12/02758 from the Spanish government.

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ROLE OF SUBSTANCE ABUSE IN PHYSICAL AND MENTAL HEALTH TRAJECTORIES THROUGHOUT THE DEPLOYMENT CYCLE: A NATIONAL GUARD STUDY.

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Aims: Identifying trajectories of health and substance abuse is fundamental to understanding risk for negative health outcomes throughout a military serviceperson's deployment cycle. This study aims to identify sub-groups of National Guard service members who are likely to be more negatively affected by deployment in the context of "citizen soldier's" dual roles.
Methods: Retrospective reports of National Guard service member surveyed approximately 2-4 months post-deployment (over 51% to Afghanistan) (N=467) were collected for one year prior to the most recent deployment, during deployment and at post-deployment. We used a latent growth mixture model using physical and mental health and substance use measures for three time periods to identify underlying trajectory groups. A multinomial mixed model was used to determine whether combat exposure, stress and other factors related to deployment predicted trajectory group membership.
Results: The best fit four-class model identified a low risk group (n=260) (group 1), a high risk for smoking group (n=122) (group 2), a medium risk for mental health problems group (n=33) (group 3) and a high risk for physical and mental health problems group (n=52) (group 4). Significant changes in physical and mental health indicators occurred among groups 3 and 4 during and after deployment. Lower levels of education and higher post-deployment alcohol use are associated with membership in group 2, while higher levels combat exposure; stress and pre-deployment family disruption are associated with membership in groups 3 and 4. Membership in group 4 was associated with higher age and lower levels of social support.
Conclusions: Results suggest that physical and mental health, as well as substance use problems, worsen during and after deployment in some groups. Combat exposure appears to affect those with comorbid conditions more severely than the substance abuse group, which suggests a distinctive role of substance abuse.
Financial Support: NIDA T32DA007313, DoDW81XWU1120108

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A PILOT STUDY OF ZOLPIDEM PHARMACOTHERAPY IN THE TREATMENT OF CANNABIS USE DISORDERS.

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Aims: Treatment admissions for cannabis use disorders (CUDs) have increased over the past 20 years. Most who enter treatment fail to quit and there are no approved medications for treating CUDs. Sleep disturbance is a hallmark feature of cannabis withdrawal and is often reported as a barrier to cessation. The present pilot study was conducted to evaluate extended-release zolpidem as a treatment for CUDs and examine the feasibility of conducting ambulatory sleep monitoring in an outpatient clinical trial.
Methods: Eighteen participants enrolled in the 12-week study, which included twice-weekly clinic visits, 12 sessions of computer-delivered psychosocial counseling (MET/CBT), case-management by an addictions counselor, and randomization to receive 12.5mg zolpidem (N=11) or placebo (N=7) for nightly self-administration. Outcome measures included urine toxicology, polysomnography (PSG), actigraphy and headband EEG sleep assessments, and self-reported substance use, sleep, and adverse events.
Results: Almost half (5/11) of participants randomized to receive zolpidem achieved a period of cannabis abstinence (verified by negative urine) during the study period; 4 were still abstinent at the end of treatment. No participant randomized to placebo achieved objectively verified abstinence. PSG assessments indicated significant sleep disturbance among study participants, however, issues related to participant compliance, equipment reliability, and lack of abstinence in the placebo group precluded our ability to evaluate the effect of zolpidem on sleep or examine relations between sleep quality and abstinence.
Conclusions: The results of this pilot study suggest that zolpidem may be a useful adjunct medication for the treatment of CUDs. Obtaining objective measures of sleep from individuals receiving outpatient treatment for CUD is difficult and requires tailored reinforcement strategies to obtain adequate levels of compliance. Further evaluation in a larger controlled trial is under way.
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SECONDARY ANALYSIS OF SMOKING RATES FROM A DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL OF MIXED-AMPHETAMINE SALTS AND TOPIRAMATE FOR COCAINE DEPENDENCE.

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Aims: This is a secondary analysis of a trial using mixed-amphetamine salts (MAS) and topiramate (TOP) for cocaine dependence. There is evidence that MAS increase tobacco smoking, and that TOP reduces the rewarding effects of nicotine. Since TOP was used adjacent to MAS, we hypothesize that there would be a difference in tobacco smoking from baseline to end of study in this group, and that this effect would be different from the placebo (PBO) group.
Methods: Cocaine dependent individuals were randomized to treatment or PBO. After a one-week PBO lead-in, patients were followed weekly for 12 weeks. All substance use was measured via timeline follow-back. A patient was a "smoker" if they smoked during the PBO lead-in. We compared the average number of cigarettes smoked per day in the lead-in week to the last full week that the patient was in the trial, and performed t-tests to see if there was a significant difference.
Results: There were 24 patient in the treatment group (MAS-TOP) and 31 in the PBO group. There was no significant difference in length of stay between the MAS-TOP and PBO group (p=0.28). Both groups achieved a significant absolute reduction in the number of cigarettes smoked at the end of the trial (MAS-TOP= -2.07 cigarettes, p=0.01; PBO= -3.372 cigarette, p= 0.04). There were no significant differences in the absolute reduction (p=0.72) or in the percent reduction (p=0.68) of cigarettes between the groups.
Conclusions: The data suggest that TOP may mitigate the expected worsening of cigarette smoking when patients are treated with MAS. With the increasing prevalence of stimulants being prescribed for attention deficit disorder, TOP may be a useful adjunct for those patients who also smoke.
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HISTORICAL REPRESENTATION OF DRUG RELATED ISSUES IN A SAMPLE OF PUERTO RICAN PRINT MEDIA.

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Aims: Stigma involves social disapproval and discrimination of individuals bearing a discrediting mark. Research on stigma has focused on individual and less on structural factors. Drug related stigma is socio-culturally constructed, influenced by media portrayals that shape public opinion. Oriented by a model of normative influences on stigma, we explored news media portrayals of drugs issues before and after the Harrison Taxation Act Amendment of 1956, that increased criminal sanctions for drug law violations. We present preliminary findings of a content analysis to assess printed media representations of the drug phenomenon, pre and post the policy change and potential implications for managing drug abuse.
Methods: We conducted a retrospective content analysis of 76 articles containing references to illicit drugs from 2 Puerto Rican newspapers. Relevant text was coded using grounded theory. Inter-coder reliability measured the consistency of coded values across researchers. ATLAS.ti software was used for data management.
Results: The dominant media portrayals involve criminal justice outcomes (16%) -arrests and incarceration are depicted as the most commons results of drug use or traffic. These representations were highly related to news content about Drug Related Crime (14%) and Drug-Control Legislation and Public Policy (15%). Adicction Health Models were largely represented in 1970's data (96%), when state regulated methadone treatment for opioid dependence was introduced. Finally, co-occurring with drug policy content the drug user was portrayed as morally deficient and a threat to society.
Conclusions: Printed media reporting shows a tendency to portray drug issues within a supply control and criminal justice frame. Dangerousness constructions are heavily represented attaching this negative attribute to drug dealers and drug users alike. Future studies should explore if portrayals differ by drug type and other social contexts. Media needs to be addressed as a relevant social instrument that may contribute to transform collective perceptions and deconstruct stigmatized representations of drug users.
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EVALUATION OF GUANFACINE ADMINISTRATION ON COGNITION IN VOLUNTEERS WITH CANNABIS-USE DISORDER.

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Aims: For study 1, to compare baseline cognitive functions between non-treatment seeking volunteers with cannabis use disorder (CBUD) vs. controls. For study 2, to determine whether guanfacine improves cognitive functions in individuals with CBUD during acute intoxication.
Methods: In study 1, in CBUD participants (N=6) vs. matched healthy controls (N=12), we are comparing cognitive functions on the N-Back, Continuous Performance Task-II (CPT), and Hopkins Verbal Learning Task (HVLT). In study 2, in CBUD participants only, we are conducting a within-subjects comparison of performance on cognitive tasks during acute intoxication with oral dronabinol (30 mg), following 7 days guanfacine (3 mg/d) treatment vs. 7 days placebo treatment.
Results: For study 1, preliminary analyses reveal CBUD participants display lower accuracy (42%) vs. controls (64%) on auditory n-back trials ($F(1,17)=4.192$, $p=0.057$). On the HVLT, CBUD participants recall fewer total words (20.8 vs. 24.0; $F(1,17)=2.559$, $p=0.129$). On the CPT, CBUD participants reaction times are 1) longer overall (59.7 vs. 53.8; $F(1,17)=2.076$, $p=0.169$), 2) quicker across the duration of the test (39.7 vs. 48.6; $F(1,17)=2.546$, $p=0.130$), and 3) quicker in response to longer inter-stimulus intervals (52.9 vs. 59.8; $F(1,17)=2.079$, $p=0.169$). For study 2, six CBUD participants have completed both phases of the double-blind trial to date, but data collection is ongoing.
Conclusions: The preliminary data from study 1 reveal the potential persistent effects of long-term high-dose cannabis use on cognitive functions, relative to controls, which are concordant with numerous studies in humans, monkeys, and rodents. For study 2, guanfacine has been well tolerated and no unanticipated adverse events have been reported to date. A primary outcome is to determine whether guanfacine affects cognition while CBUD individuals are acutely intoxicated.
Financial Support: Supported by a Seed Grant (CDV) from, and conducted at, the Michael E. DeBakey VA Medical Center, Houston, TX

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CURRENT MARIJUANA USE AND CARDIOMETABOLIC DISEASE RISK IN UNITED STATES EMERGING ADULTS, 2005-2010.

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Aims: To examine the relationship between current marijuana use and cardiometabolic disease risk factors (CMDR) stratified by body mass index (BMI) in a United States population-based sample of 20-to-30-year olds.
Methods: The sample (N=5,674) included 20-to-30-year olds who completed the National Health and Nutrition Examination Survey between 2005 and 2010. Current marijuana use was categorized based on last 30 days use as follows: light (1-3 days), regular (4-14 days), and heavy (≥15 days). CMDR included elevated fasting glucose and insulin, triglycerides, systolic and diastolic blood pressure, highly sensitive C-reactive protein, total and low-density lipoprotein cholesterol, serum cotinine, waist circumference, and low high-density lipoprotein cholesterol. Logistic regression models were used to assess the relationships between current marijuana use and a cluster of three or more CMDR present among the whole sample and then stratified by CDC defined BMI categories: normal weight (BMI < 25 kg/m^2), overweight (BMI ≥ 25 kg/m^2), obese (BMI ≥ 30 kg/m^2), and severely obese (BMI ≥ 35 kg/m^2).
Results: Over one third of regular (34.9%) and heavy (36.5%) current marijuana users compared to 22.1% of never users had ≥ 3 CMDR present ($p=0.01$ for both contrasts). The odds of having ≥ 3 CMDR significantly increased with degree of marijuana use for both normal weight (OR 2.58, 95% CI:1.45-4.59, for light use, OR 3.48, 95% CI:1.95-6.22, for regular use and OR 3.42, 95% CI:2.03-5.75, for heavy use, $P<0.001$ for all) and severely obese (OR 3.63, 95% CI:1.31-10.08, for light use, OR 10.58, 95% CI:2.21-50.60, for regular use and OR 11.21, 95% CI:2.37-52.95, for heavy use, $P<0.01$ for all) emerging adults.
Conclusions: Results suggest a possible dose-response relationship with degree of marijuana use and cardiometabolic disease risk among normal weight and severely obese emerging adults.
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UNIQUE FACTORS ASSOCIATED WITH YOUNG WOMEN IN SUBSTANCE USE TREATMENT: CRAVING, IMPULSIVITY, EMOTION REGULATION, AND PHYSIOLOGICAL RESPONSE.

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Aims: In nonclinical samples, young women have been shown to be more dependent on alcohol and perceive less need to enter treatment when compared to older women (Wu & Ringwalt, 2004). Upon entering treatment, young women are more likely to drop out (Copeland & Hall, 2006) and generally have poorer treatment outcomes (Satre et al., 2004) than older women. Examination of factors that may explain treatment dropout and poorer treatment outcomes in younger women are needed.
Methods: The present study examined differences between three age groups of women (18-25, 26-40, and 41-65) on multiple characteristics including trauma symptoms, anxiety, depression, alcohol dependence, craving, impulsivity, emotion regulation, and both self-reported craving and salivation following a cue reactivity procedure.
Results: The sample (n=56) was assessed at entry to a residential substance use treatment program, had a mean age of 32.41 (SD=10.16), and was 85.7% Caucasian. The entire sample had a current diagnosis of PTSD, 98.2% were alcohol dependent, and 96.4% were drug dependent. Group differences were examined with one-way ANOVAs and any significant differences were examined with Bonferroni posthoc analyses. Results indicated young women reported significantly higher scores on the following measures when compared to older women: impulsivity ($p=.01$), difficulty regulating emotion ($p=.02$), craving ($p=.02$), and both self-reported craving ($p=.02$) and salivation ($p=.03$) following the presentation of combined trauma and alcohol cues.
Conclusions: These findings suggest younger women, despite not differing from older women on level of alcohol dependence and trauma symptoms, reported significant elevations on multiple variables. Young women presenting to substance use treatment may benefit from interventions specifically targeting some of these areas (e.g., impulsivity and emotion regulation), as well as additional interventions for craving, which could lead to increased treatment retention and better treatment outcomes.
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BDNF LEVELS OF CRACK USERS ARE ASSOCIATED WITH CLINICAL OUTCOME DURING INPATIENT TREATMENT.

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Aims: The aim of this study was to evaluate whether BDNF levels before and after detoxification are related to better clinical outcome during inpatient treatment.
Methods: Serum BDNF was evaluated in 41 male crack users on the first and in the last day of hospitalization in an addiction clinic. Clinical improvement was assessed through medical record chart reports at discharge, based on clinical evaluation. Serum BDNF was assayed using a sandwich ELISA kit. Student's t-Tests (parametric) and Wilcoxon Rank Sum test (non-parametric) were performed to compare mean and median between groups.
Results: Results: 27 crack users were described as "improved" and 14 as "not improved" while hospitalized. BDNF level before detoxification was lower ($p< 0.001$) in the first group (23.1±10.5 ng/mL) in relation to the "not improved" group (36.3±5.2 ng/mL). However, patients with better outcome had their BDNF levels increased in a much higher proportion at hospital discharge [median 41.3% and interquatile range(IR) 8.2% to 96.0%] than those with a poorer outcome (0.82% IR -14.2% to 21.0%).
Conclusions: Our results suggest that crack users with worse treatment outcome could have impairment in their brain plasticity, specifically related to neurogenic and neurotrophic properties which are important to cognitive and addiction recovery. We hiphotesize that these original findings may help develop tailored psychosocial and pharmacologic strategies according neurobiological (ex. BDNF levels) characteristics of drug addicted in the future.
Financial Support: Brazilian Government - Secretaria Nacional de Políticas sobre Drogas

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INFLUENCE OF NICOTINE REPLACEMENT THERAPY ON HEART RATE VARIABILITY AND RELAPSE.

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Aims: Research has shown nicotine replacement therapy (NRT) to increase heart rate variability (HRV) in smokers and increased HRV has been shown to negatively predict relapse. The present study investigates the relationship between HRV and relapse across multiple doses of NRT.
Methods: Participants were 24 tobacco smokers (17 male, 7 female) who were not seeking treatment. After overnight abstinence, they received NRT dose (0mg, 7mg, 21mg, 42mg) in a randomized double-blind fashion with each receiving 3 of 4 possible doses on different days, 1 week apart. No smoking was allowed during the study day. Time domain HRV variability was measured using a three-channel ECG during presentations of cigarette cues (a lit cigarette), which occurred during 1-hour intervals at 7 time points. Relapse was measured as the amount of money a subject would pay to smoke at the end of the research day. Participants who paid more could smoke sooner. Additionally, we measured nicotine levels at the end of each research day and breath CO levels the following afternoon.
Results: In the 0, 7 and 21 mg NRT conditions, HRV was shown to significantly increase over time, $F(2, 23) = 4.616$, $p = .021$. No significant time effect was found in the 42 mg NRT condition. During cue presentation, HRV decreased dose-dependently across all NRT conditions, $F(3,21) = 7.64$, $p = .001$. Relapse rates decreased dose-dependently $F(2,21) = 4.042$, $p = .01$ with relapse rates lowest at the 42 mg dose. There was a significant correlation between decrease in HRV and relapse ($r = .29$, $p < .05$). Relapse was also negatively correlated with nicotine levels ($r = -.25$, $p < .05$). End of day nicotine levels were negatively correlated with CO measures ($r = -.285$) the following day.
Conclusions: NRT may increase HRV in smokers during smoking cessation, but lower levels of HRV may be found with higher NRT doses and higher NRT doses may lead to lower relapse. Our preliminary results challenge the common notion that increased HRV is protective against relapse.
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FUNCTIONAL APPROACH IN MODELING DRUG DEPENDENCE PROCESSES (THEORETICAL OVERVIEW MIDWAY TO FINAL RESULTS).

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Aims: In this theoretical overview of statistical modeling research now underway, we describe a stage-transition model from drug use to dependence, with an "input-response" curve (x-axis is days of drug use; y-axis is probability to observe dependence). Standard dose-response models might be sigmoid, with early perturbation by a feedback loop (e.g., if the dependence process kicks in early, and starts to drive up the count of drug-using days). We aim to quantify this departure from "S"-shape curves and to shed new light on potentially important feedback loops in early drug dependence processes as studied in clinical and pre-clinical research.
Methods: One model for functional relationships between counts of days of drug use and the dependence level is based on a Hill function — a function often used with sigmoid curves. What results is a nonlinear model with advantages over typical generalized linear models for sigmoid curves (e.g., binomial GLM with logit link). The Hill function derives from a known mathematical function describing physical phenomena, and yields estimates of readily interpretable parameters such as an inflection point in a sigmoid curve as might be seen when drug dependence drives up days of drug use.
Conclusions: Mathematical functions to describe dose-response relations are used widely in pharmaceutics and pharmacokinetics research, but functional modeling largely has been ignored in human field studies of drug dependence processes, with errors of inference whenever counts of drug-using days are assumed to be exogenous 'dose levels'. These counts might well be endogenous and reactive once processes of becoming drug dependent take form. Applying these ideas, we intend to provide functional parameter estimates and interpretations for different internationally regulated drugs such as cannabis and cocaine, with later application in evaluation of early effects of prevention and early intervention programs.
Financial Support: Supported by NIDA T32DA021129 (OAV); K05DA015799 (JCA).

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DEPRESSIVE SYMPTOMS AND IMPULSIVITY AMONG TRAUMA-EXPOSED, COCAINE-DEPENDENT ADULTS: ASSOCIATIONS WITH HIV-RELEVANT DRUG AND SEX RISK BEHAVIORS.

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Aims: This investigation examined the main and interactive effects of depressive symptoms and impulsivity with regard to HIV-relevant drug and sex risk behaviors: (1) intravenous (IV) drug use, (2) condom use frequency, (3) number of sexual partners in the past six months, and (4) worry about HIV infection. It was hypothesized that heightened levels of depressive symptoms and impulsivity (and their interaction) would be associated with greater levels of each of the outcomes, above and beyond the main effects and covariates. Trauma exposure severity was included as a covariate; substance use severity was not included as a covariate since it was not significantly associated with the outcomes at the zero-order level.
Methods: Participants were comprised of 78 (11 women; Mage = 44.3; SD = 11.2) trauma-exposed, cocaine-dependent adults presenting to an addictions research center in a large urban area; data collection is ongoing. Participants were administered diagnostic interviews, provided urine samples to confirm active substance use, and completed self-report questionnaires.
Results: A series of hierarchical and logistic regression analyses was conducted. The interactive effect of depressive symptoms by impulsivity was significantly associated with IV drug use, frequency of condom use, and worry about HIV infection (p's $< .05$). Depressive symptoms were significantly incrementally associated with IV drug use, condom use frequency, and worry about HIV infection (p's $< .05$). Impulsivity was significantly incrementally associated with condom use frequency ($p < .05$), while associations with IV drug use and number of sexual partners approached significance (p's = .05).
Conclusions: Specialized interventions targeting depressive symptoms and impulsivity may be more successful in achieving risk reduction in this difficult-to-treat population. Clinical implications and future directions will be discussed.
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CORRELATES OF PRESCRIPTION DRUG MARKET INVOLVEMENT.

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Aims: Prescription drug misuse among young adults has increased within the U.S. over the past decade. While research has focused on correlates of misuse, less research has taken prescription drug dealing as the object of analysis. Involvement in prescription drug markets remains an important subject.
Methods: We use data collected from 404 young adult prescription drug misusers sampled from urban nightlife scenes. Using logistic regression models, we examine both recent prescription drug selling and recently being approached to sell prescription drugs. We predict these outcomes using demographic characteristics, personal prescription drug misuse, and nightlife scene involvement.
Results: For prescription drug selling, those from a self-identified "rich" parental class were more likely to sell compared to all other social classes. Heterosexuals had higher odds (OR=5.86) of selling. Both more frequent misuse of sedatives (OR=1.03) and having a prescription for stimulants (OR=4.14) are associated with higher odds of selling. Finally, involvement in college bar scenes increases the odds of selling by 2.47. As for being approached to sell prescriptions, males (OR=2.07), more frequent stimulant users (1.03), and those with prescriptions for sedatives (OR=2.10) have higher odds of being approached. Similar to selling, those in the college bar scene had 2.12 higher odds of being approached to sell.
Conclusions: Of seven nightlife scenes, college bar scene involvement was the only site associated with both selling and being approached to sell, net of personal education level. Thus, regardless of education level, participation in the college bar scene appears to provide a network for prescription drug markets. Heterosexuals had significantly higher odds of drug selling relative to their sexual minority peers. Having prescription access and frequency of use, specifically related to sedatives and stimulants, are associated with involvement in prescription drug markets. Given the physiological dependence that can be associated with painkillers, such misusers may be less likely to sell their drugs.
Financial Support: NIDA R01DA025081

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PAIN SENSITIVITY AND TOLERANCE AMONG INDIVIDUALS ON OPIOID MAINTENANCE: LONG-TERM EFFECTS.

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Aims: Medication assisted treatment with opioids for opioid dependence alters the pain experience. The purpose of this study is to 1) evaluate changes pain sensitivity and tolerance with these opioid treatments; 2) identify the duration of this effect after treatment cessation, and 3) assess pain differences between partial mu-agonists (buprenorphine) or a full mu-agonists (methadone) treatments.
Methods: One hundred and twenty individuals were recruited in 4 groups (n=30): 1- current methadone for opioid addiction; 2- current buprenorphine for opioid addiction; 3-history of opioid agonist treatment for opioid addiction but with current prolonged abstinence of opioids (M=121 weeks;SD=23.3);and 4-opioid naïve. Participants completed a psychological assessment and a cold water task. Time to first pain report (sensitivity) and time to disengagement from the pain task (tolerance) were recorded. Time to event analyses were used.
Results: A Kaplan-Meier showed significant group differences for both pain sensitivity (LR=15.5;p<.01) and tolerance (LR=20.11; p<.001). A follow up Cox, found that any current or historical use of opioid maintenance resulted in significant differences in pain sensitivity compared to the opioid naïve (p's<.01). Pain tolerance was better for those with a history of opioid maintenance compared to active methadone patients (p<.05), and the highest tolerance was found among the opioid naïve (p's<.001). Correlations of the prolonged abstinent group, showed pain tolerance was significantly improved as the weeks since last opioid dose increased (R=.37;p<.05); but did not alter sensitivity.
Conclusions: Among individuals with a history of prolonged opioid treatment, there appears to be long-term differences in pain sensitivity that do not resolve with discontinuation of opioid treatment. Although sensitivity does not change, tolerance to pain does appear to increase after the completion of treatment. This has significant implications for treating individuals with co-morbid opioid addiction and pain, including both chronic pain and acute pain conditions.
Financial Support: This study was supported by NIDA grant K23DA030397(AW)

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CONDITIONED TASTE AVOIDANCE INDUCED BY Δ-9-TETRAHYDROCANNABINOL IN THE FISCHER AND LEWIS RAT STRAINS.

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Aims: Although the inbred Fischer (F344) and Lewis (LEW) rat strains differ in their sensitivity to the rewarding effects of THC, no data have been reported on differences in their sensitivity to the drug's aversive effects, a limiting factor in drug use and abuse. Given that the balance of the rewarding and aversive effects of drugs impact their use and abuse, examining the degree of differences in such effects may help characterize possible genetic factors important to abuse vulnerability.
Methods: The aversive effects of THC (1-5.6 mg/kg; IP) were examined in 32 F344 and 32 LEW subjects using the conditioned taste avoidance (CTA) procedure. Every fourth day for five trials animals of both strains were given a novel saccharin solution to drink followed by an injection of THC or its vehicle. Given the association between core body temperature and the acquisition of CTAs, thermoregulation was assessed following an acute injection of THC (same as CTA groups) after a week washout period following the last trial.
Results: Subjects in both strains displayed dose-dependent THC-induced taste avoidance, with no significant strain difference. THC induced dose-dependent decreases in core body temperature in both strains. LEW subjects displayed lower core body temperatures than F344 rats, although this effect was independent of THC and was likely stress related.
Conclusions: Although the strains differ in CTA to a host of drugs (i.e., display differential CTAs), there are exceptions (including THC). The similarity among these exceptions is that each induces rejection responses in taste reactivity tests, suggestive that these compounds may induce emesis. That the two strains do not differ in taste avoidance induced by THC and these other compounds suggests that these strains are not differentially sensitive to their emetic effects. Understanding the extent to which these strains differ in their sensitivity to the aversive effects of various drugs may provide insight into their abuse vulnerability.
Financial Support: This research was supported by a grant to ALR from the Mellon Foundation at American University.

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CHARACTERIZATION OF MORPHINE DISCRIMINATIVE STIMULUS PROPERTIES IN C57BL/6 MICE.

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Aims: The discriminative stimulus effects of morphine have not yet been well characterized in mice. Therefore, the purpose of the present study was to establish and characterize morphine discrimination in a commonly utilized mouse strain.
Methods: Adult male C57BL6/J mice were trained to discriminate 5.6 mg/kg morphine (s.c., 30 min pretreatment) from vehicle for food reinforcement using a two-choice operant task.
Results: After demonstrating stimulus control, a morphine generalization test was conducted. Orderly, dose-dependent generalization was observed with a calculated ED50 of 2.08 mg/kg (95% CI: 1.53-2.83). A time course evaluation revealed full substitution at 30 and 60 min, and roughly 50% morphine-like responding at 120 min. Naltrexone dose-dependently blocked the morphine discriminative stimulus. Heroin fully substituted for morphine (ED50=1.03 mg/kg; CI: 0.68-1.58). Neither the kappa agonist U50,488 nor THC substituted for morphine, even at doses that decreased responding compared to vehicle.
One disconcerting issue was that subjects did not become tolerant to the rate-suppressant effects of the 5.6 mg/kg training dose. In an attempt to resolve this, a second morphine dose response curve was established and the training dose was faded to 3.0 mg/kg based on its lack of rate-suppressant activity. Morphine and heroin dose-response curves were reestablished with this new training dose, yielding ED50s of 1.83 mg/kg (CI: 0.90-3.72) and 0.30 mg/kg (CI: 0.23-0.38), respectively. Lastly, buprenorphine dose-dependently substituted for morphine (ED50 = 0.03 mg/kg; CI: 0.03-0.04 mg/kg) without affecting response rates.
Conclusions: The findings of the study are in agreement with results from other species. Despite fading the training dose to 3.0 mg/kg, inconsistent rate-suppression was still observed, suggesting that tolerance had not developed fully to the rate-decreasing effects of morphine. Taken together, these data indicate that morphine discrimination can be established in mice and that this model may have utility in identifying drugs with morphine-like abuse liability.
Financial Support: Supported by N01DA128904 to LSH.

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FATAL AND NON-FATAL OVERDOSE AFTER NARCOLOGY HOSPITAL DISCHARGE AMONG HIV-INFECTED RUSSIANS.

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Aims: The estimated incidence of fatal overdose among Russians who use drugs is 0.22 per 100 person-months. In Russia, medically managed withdrawal (detox) is provided by state-supported narcology hospitals, where 40% of patients are HIV-infected and relapse rates are as high as 90%. Detox initiates opioid abstinence, decreases tolerance, and thus increases overdose risk when relapse occurs. In this study, we estimate fatal and non-fatal overdose probabilities following discharge from narcology hospital among Russians with HIV infection and injection drug use (IDU).
Methods: We prospectively followed narcology patients with HIV and IDU after discharge. Fatal overdose was determined based on emergency contact reports to study staff. Non-fatal overdose was self-reported at the 3-month assessment. We used the Kaplan-Meier method to estimate the cumulative probabilities of any overdose and a fatal overdose.
Results: Of 263 narcology patients with HIV infection and IDU, 26% were female, median age was 33.7 years, and any previous non-fatal overdose was reported at baseline by 30%; the median follow-up time was 3.3 months. During follow-up, 21 subjects experienced any overdose, 7 of which were fatal resulting in estimated probabilities of 15.3% (95%CI: 8.7-26.3) for any overdose (fatal or non-fatal) and 3.7% (95%CI: 1.5-8.6) for a fatal overdose. Among 14 individuals with non-fatal overdose, 33 overdose events were reported. Five of the 7 overdose deaths occurred prior to the 3-month assessment. The fatal overdose incidence was 0.62 per 100 person-months (95%CI 0.29-1.30).
Conclusions: Overdose among patients with HIV and IDU is common after narcology hospital discharge. The incidence of fatal overdose appears greater than the overall high incidence of overdose deaths among Russians with IDU. Overdose prevention interventions are warranted among Russian narcology patients with HIV infection.
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ASSOCIATIONS BETWEEN CHILDHOOD MALTREATMENT, INTIMATE PARTNER VIOLENCE, AND SUBSTANCE USE DISORDERS.

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Aims: Intimate partner violence (IPV) has been associated with increased risk for substance use disorders (SUDs). Individuals with histories of childhood maltreatment (CM) are at increased risk for both IPV and SUDs in adulthood. However, no nationally representative studies have examined the joint effect of CM and IPV on risk for SUD. We hypothesized that: 1) CM and past-year IPV would be associated with increased odds of past-year SUD, and 2) men and women with both CM and IPV would have increased risk for SUD relative to those with one or neither exposure. We also examined whether associations vary as a function of gender.

Methods: Men and women in wave 2 (2004-2005) of the National Epidemiologic Survey of Alcohol and Related Conditions (N = 34,653) provided data on CM, past-year IPV, and past-year SUD. SAS 9.3 was used for logistic regressions that accounted for sample weights, stratified by gender, and adjusted for age, education, and employment.

Results: Approximately 32% reported CM, 6% reported past-year IPV, and 11% reported past-year SUD. Men and women exposed to CM had 2.0 (95% CI=1.88-2.20) and 2.5 (95% CI=2.28-2.76) times the odds of IPV, and 1.70 (95% CI=1.61-1.80) and 2.40 (95% CI=2.23-2.58) times the odds of SUD, respectively. Men and women reporting IPV had 2.29 (95% CI=2.12-2.48) and 3.38 (95% CI=3.09-3.71) times the odds of SUD, respectively. Relative to men without CM or IPV, the odds of SUD were 3.12 (95% CI=2.78-3.51) for men with CM and IPV and 1.68 (95% CI=1.57-1.78) for men with either CM or IPV. Relative to women without CM or IPV, the odds of SUD were 5.79 (95% CI = 5.14-6.53) for women with CM and IPV and 2.38 (95% CI = 2.15-2.63) for women with either CM or IPV.

Conclusions: Consistent with expectations, CM was associated with an approximately 2-fold increase in IPV and SUD. IPV was associated with a 2-fold increase in SUD for men and a more than 3-fold increase in SUD for women. Those with CM and current IPV had increased odds of past-year SUD relative to those with one or neither exposure, and associations were generally stronger for women than for men.

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SUBSTANCE USE TRAJECTORIES AMONG DRUG-USING YOUTH PRESENTING TO AN URBAN ED.

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Aims: A visit to an urban emergency department (ED) provides an opportunity for intervention for drug-using youth, which may be especially salient for those presenting with assault. This paper examined longitudinal substance use trajectories among drug-using youth presenting the ED.

Methods: Assault-injured youth (ages 14-24) endorsing drug use (n=350), and a proportionally-sampled comparison group (n=250) endorsing drug use, completed a baseline assessment (e.g., CTS-2, timeline follow back calendar) and follow-ups at 6, 12, 18, and 24 months. Trajectory analyses examined the number of days of substance use (i.e., binge drinking, marijuana, other illicit drugs, or prescription opioid, sedative, or stimulant misuse) over the 2 year follow-up. Subsequent analyses examined baseline markers of substance use trajectory groups.

Results: Trajectory analyses identified 4 groups: Low Decreasing (31.8%; n=191); Low Increasing (18.0%; n=108); Moderate Decreasing (16.3%; n=98); and Moderate Increasing (33.8%; n=203). Mean days of substance use from baseline to 24 months was: 7.9 - 3.0 (Low Decreasing), 12.5 - 47.0 (Low Increasing), 20.9 - 8.1 (Moderate Decreasing), and 22.8 - 71.6 (Moderate Increasing). Males were less likely to be in the Low Decreasing group than the other groups. At baseline, as compared to the Low Decreasing group, other trajectory groups reported significantly more peer and dating aggression, gun carriage, antisocial personality disorder, negative peer influences, and community violence; substance use trajectory groups were not associated with age, race, reason for ED visit, peer or dating victimization, PTSD, anxiety, depressive symptoms, and peer positive influences.

Conclusions: Data support the need for specialized interventions for drug-using youth presenting to an urban ED, particularly those involved with aggression and gun carriage, as these youth have more severe substance use trajectories.

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INCREASED VENTRAL STRIATUM ACTIVATION IN RESPONSE TO HEROIN CUES IN HEROIN-DEPENDENT WOMEN AFTER EXTENDED-RELEASE NALTREXONE INJECTION.

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Aims: Brain and behavioral responses to drug-related cues are potential markers of addiction treatment effects. We hypothesized that sex differences in the response to heroin cues during treatment of heroin addiction with extended-release opioid antagonist naltrexone (XRNTX) are detectable by functional magnetic resonance imaging (fMRI).

Methods: We studied 32 heroin-dependent patients (aged 29.06 ± 8.47,15F). Following detoxification, participants received up to 3 monthly XRNXT injections. fMRI was performed immediately before (PRE_XRNTX) and 1-2 weeks after (ON_XRNTX) the first XRNTX. During fMRI, participants viewed heroin-related images (cues). Other variables included change in craving after cues exposure, plasma levels of naltrexone and metabolites at three time-points during the XRNTX and a urine drug screen (UDS) positive for common illicit drugs.

Results: 19 (59%) participants (7F) completed the study. There were no sex differences in cue-induced heroin craving ($t(30)=0.759$, $p=0.454$) and withdrawal before and during XRNTX or naltrexone plasma levels between the injections. Comparing brain responses to heroin cues ($z \geq 1.64$, uncorrected) PRE and ON_XRNTX, we found increased activation in the bilateral ventral striatum in women and decreased activation in the right hippocampus in men.

Conclusions: Lack of sex differences in craving after XRNTX and the higher drop-out rate in women suggest that fMRI may be more sensitive measure of XRNTX treatment response than subjective measures. Increased ventral striatum activation after XRNTX in women points to the potential mechanism of lower adherence to treatment in heroin-dependent females.

Financial Support: US–Netherlands Bi-National Collaborative Research on Drug Abuse Administrative Supplement to DA024553-05 R01, Analytical Services Program of the National Institutes of Health and the Veterans Administration. Study medication (XRNTX, Vivitrol®) was provided by Alkermes Inc. through Investigator-Sponsored Study (ISS) grant.

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CHANGE OF SUICIDALITY AMONG HEROIN USERS: 1 MONTH AFTER METHADONE MAINTENANCE TREATMENT.

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Aims: Suicide is a leading cause of death among heroin users. Factors affecting suicidality during treatment remain unclear.This study aimed to investigate the heroin users' suicidality before and after 1 month of methadone maintenance treatment (MMT). Factors associated with change in suicidality were also explored.

Methods: A total of 597 newly admitted MMT patients were recruited from 8 hospitals located in the northern and mid-Taiwan. Demographics, and history of substance abuse and treatment were obtained from medical records. Suicidality was assessed by research nurses using suicidality module of Mini International Neuropsychiatric Interview (MINI). After the first month of MMT, subjects retained in treatment were re-assessed for their suicidality. Logistic regression analyses were used to determine the factors linked to change in suicidality during the first month of MMT.

Results: Among the 389 patients with suicidality reassessment, 83 (21.3%) improved, and 58 (14.9%) worsened or had no improvement for their suicide risk. Contrast to the 248 subjects with no suicidality during the past 1 month of MMT, those with no improvement were significantly associated with no full-time job (e.g., part-time job: OR= 6.0, $p<0.001$; unemployed: OR= 7.5, $p<0.001$), financial difficulty (e.g., loan from others: OR=2.6, $p<0.01$; social welfare support: OR=13.0, $p<0.01$), HIV-infected (OR=2.8, $p<0.01$), and recent use of methamphetamine (OR=1.1, $p<0.01$). On the other hand, the improving group was significantly associated with HIV-infected (OR=2.1, $p<0.05$), and use of antidepressant before MMT (OR=3.3, $p<0.01$) relative to those with no suicidality during the past month.

Conclusions: The MMT will help heroin users to reduce suicide risk. However, service providers should pay attention to those with problems of unemployment, financial difficulty and concomitant use of other illicit drugs.

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A HYPER-CONNECTED AND RESILIENT SMALL-WORLD NETWORK IN THE COCAINE-DEPENDENT BRAIN.

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Aims: Functional connectome (FCON) has been a hot research topic and its alterations have been shown in several brain disorders. This study was performed to test the hypothesis that the addicted brain may have changes in FCON.
Methods: Resting state fMRI images were obtained from 43 cocaine users (COC), and 25 age and education matched normal controls (MC). After motion correction, images with large motions were discarded. The rest of them were filtered, and registered into the MNI space. Mean fMRI timecourses were extracted using an anatomical atlas and FCON was generated based on the inter-regional correlation coefficients (CC) with a threshold varied from 0.01~0.6. FCON properties including wiring cost, degrees of segregation and integration were calculated using the graph theory analysis. Network resilience was simulated by re-calculating network properties after sequentially removing brain subdivisions according to their connection degrees from high to low. Two-sample t-tests were used to assess MC-COC FCON difference. The association between FCON properties and cocaine dependence as defined by ASI was examined using linear regression. Age and other drug dependence were included as nuisance covariates.
Results: As compared to MC, COC showed a higher network wiring cost, but with higher communication efficiency; COC' FCN was more functionally integrated but less segregated, with a reduced small-worldness, and more resilient to simulated targeted attacks (all $p<0.05$ corrected). Small-worldness in patients was linked ($p=0.043$) to cocaine dependence severity.
Conclusions: These findings suggest that the cocaine-addicted brain is in a highly "tuned" communication state that enables a rapid, semi-automatic, execution of goals. This might help to explain both the clinical phenomenology of the disorder (ritualized, efficient pursuit of drug), and the difficulty in attempting to target these connections with treatment interventions. FCON analysis may be useful for characterizing addiction, and a screen for potential anti-addiction therapeutics.
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CORRELATES OF RISK FOR PRENATAL ALCOHOL USE AMONG WIC RECIPIENTS.

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Aims: Large disparities exist in prenatal alcohol use with 24% of Medicaid-eligible pregnant women reporting prenatal alcohol use. Prenatal alcohol use puts mothers and their children at risk for pregnancy, birth, and neonatal complications including a leading known cause of brain damage, developmental disabilities, and birth defects in children, known as fetal alcohol spectrum disorders. In addition, prenatal alcohol use and smoking combined produce the worst birth outcomes. The current study examined demographic variables and other substance use patterns as characteristics of low-income pregnant women at risk for prenatal alcohol use.
Methods: We conducted brief survey for 140 pregnant women at offices of Special Supplemental Nutrition Program for Women, Infants, and Children (WIC). At present, over 95% of women who acknowledged being pregnant have responded to the survey, and 27% have been identified as being at risk for prenatal alcohol use (n=38) based on scores from the TWEAK.
Results: Preliminary findings indicate that lifetime homelessness ($p < 0.001$), smoking status ($p < 0.001$), having a history of marijuana use ($p = 0.001$), and having a history of illicit drug use ($p = 0.036$) were significantly associated with risk for prenatal alcohol use. When these variables were included in a multivariate model, only lifetime homelessness ($p = 0.009$) and smoking status ($p = 0.002$) remained significantly associated with at risk status.
Conclusions: Our preliminary findings corroborate earlier studies examining the risk for prenatal alcohol use among economically disadvantaged women and underscore the need for comprehensive services, including housing support and other treatment services, for them.
Financial Support: 5P50DA027841

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IDENTIFYING PRESCRIPTION DRUG MISUSE IN PRIMARY CARE PATIENTS: A TALE OF TWO INSTRUMENTS.

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Aims: The present study: 1) examined prevalence of prescription medication misuse in an urban primary care clinic; and 2) compared two screening instruments modified to focus on prescription medication misuse in a medical care setting.
Methods: Primary care patients attending an urban hospital-based clinic completed an anonymous computer-directed health screen and RA-administered survey (total: 20 min) while waiting to see the doctor. Domains included: demographics, tobacco, alcohol/other drug use and medical/psychosocial concerns (e.g., mood, sleep, pain). The 13-item RA screener included 4-item RxCAGE (CAGE modified to focus only on prescription medications) and 6-item Prescription Opioid Misuse Index (POMI) expanded to include other prescription drugs (Knisely et al., 2008). Item frequencies and scale scores for the 2 screeners were calculated. Sensitivity and specificity of POMI-e were derived relative to RxCAGE. Additional analyses will compare screen positive and negative participants on medical and psychosocial concerns in the computerized survey.
Results: Participants were N= 2,330 patients. Demographically, 77.3% were female, 71.0% were African-American, and mean age was 46.8 years (SD 11.8). Over one-third (34.8%) of the sample said yes to at least one RxCAGE item and 14% answered yes to 2+ items. Item endorsement ranged from felt guilty (8.1%) to tried to cut down (21.2%). On the expanded POMI (POMI-e), 33.6% answered yes to at least one item and 17.6% answered yes to 2+ items. Lowest frequency item was going to >1 doctor (4.6%) and highest frequency was using the medication to feel good (15.1%). Relative to RxCAGE, POMI-e sensitivity was 53.5% (positive likelihood ratio: 4.57) and specificity was 88.3% (negative likelihood ratio 0.53).
Conclusions: Rates of prescription medication misuse were substantive. The 2 instruments, one general (RxCAGE) and one more specific (POMI-e), both showed promise as screening tools and warrant further study.
Financial Support: Financial Support: RO1 DA026091

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IMPAIRED DRIVING HISTORIES AMONG RURAL FEMALE DRUG-INVOLVED OFFENDERS.

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Aims: Although overall arrests for impaired driving decreased over the past decade, the number of females arrested for impaired driving has increased 21%, far surpassing the 3% increase for all female arrests (FBI, 2013). Despite this increase in arrests, there is limited research on female impaired drivers, particularly those from rural areas. The present study adds to this limited information by examining impaired driving histories in a sample of rural female drug-involved offenders.
Methods: As part of a larger study on drug use and high risk behavior among rural women, 136 females from three rural jails were randomly selected, screened, and consented. During a baseline face-to-face interview, participants were asked about the number of times in the past year they had driven impaired and about the specific types of drugs involved.
Results: Three-fourths (75%) of participants reported driving impaired in the past year with a median of 150 impaired driving episodes among impaired drivers, and 6.6% of participants were currently in jail because of an impaired driving arrest. The majority of impaired drivers reported driving under the influence of drugs in the past year (96.1%) with fewer reporting alcohol-impaired driving (33.3%). Among impaired drivers, 80.4% drove under the influence of a prescription opioid, 33.3% a benzodiazepine, and 15.7% marijuana. Cocaine, heroin, and methamphetamine impaired driving were less prevalent (< 4%). When impaired drivers were compared to other participants, no significant differences were found for age, race, education, or marital status. However, impaired drivers were more likely to have been the passenger of an impaired driver in the past year (73.5% vs. 52.9%, $p < .05$), usually their male partner.
Conclusions: Findings highlight the high rates of impaired driving among rural female drug-involved offenders, particularly while under the influence of prescription opioids, benzodiazepines, and alcohol. Implications for public health and the prevention and intervention of this dangerous risk behavior will be discussed.
Financial Support: NIDA R01DA033866 and T32DA035200

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COMPARISON OF BACLOFEN VS. NALTREXONE TREATMENT DURING ABSTINENCE ON REINSTATEMENT OF ALCOHOL SELF-ADMINISTRATION IN BABOONS.

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Aims: The GABA-B receptor agonist, baclofen, is under investigation as a potential alcohol use disorder (AUD) treatment to prevent relapse to drinking. Previously, we have also shown acute doses of baclofen reduced self-administration responses and total g/kg alcohol intake under daily alcohol access, and facilitated extinction of alcohol seeking responses. We have also shown alcohol abstinence results in a transient increase in alcohol seeking and self-administration on the first day of return to alcohol access (alcohol deprivation effect, ADE) and then resumption of heavy alcohol intake. The aim of the current study was to determine if chronic baclofen treatment initiated and maintained during alcohol abstinence would decrease alcohol seeking and self-administration upon return to alcohol access. Naltrexone was tested as a positive control.
Methods: In the current study, baboons self-administered alcohol under a chained schedule of reinforcement (CSR). The CSR consisted of 3 separate "linked" components, each associated with distinct stimuli (cues) and different behavioral contingencies (schedule requirements) leading to the opportunity to self-administer 4% w/v alcohol. Under baseline conditions, baboons self-administered an average of 1 g/kg alcohol in a 2-hr period. Each dose of baclofen (0.1-1.8 mg/kg) or naltrexone (0.3- 5.6 mg/kg) was administered daily beginning on day 1 of a 5-day forced abstinence period and treatment was continued for 5 days of alcohol access (i.e., 10 days total treatment). Stable baseline alcohol self-administration was then reestablished and maintained for at least 2 weeks before the next treatment/abstinence period.
Results: When compared to vehicle, baclofen did not prevent ADE on day 1 and did not reduce alcohol seeking or self-administration across the treatment period. In contrast, naltrexone attenuated ADE on day 1 and reduced subsequent alcohol seeking and self-administration across treatment days.
Conclusions: These data do not support the use of baclofen during early abstinence to reduce relapse to heavy drinking.
Financial Support: NIAAA R01AA015971

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A PET IMAGING STUDY ON THE EFFECTS OF TREATMENT WITH MODAFINIL AND TOPIRAMATE ON BRAIN MECHANISMS UNDERLYING COCAINE DEPENDENCE IN CONCURRENT COCAINE-AND HEROIN-DEPENDENT PATIENTS.

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Aims: To investigate the effects of modafinil and topiramate on 1) drug use 2) dopamine receptor D2 binding potentials (BP) in the striatum using [11C] raclopride in PET and 3) on cue-induced craving as measured both in subjective ratings and in regional cerebral glucose metabolism (rCMRglc) using [18F] -Fluorodeoxyglucose (FDG) in PET .
Methods: We used PET brain imaging to monitor treatment progress with modafinil (n = 5) or topiramate (n = 5) in male outpatients concurrently dependent on cocaine and heroin. They were assessed before treatment and after 4 weeks of pharmacotherapy plus counseling. Outcome measures included drug use measured by urine testing, drug craving, brain dopamine D2 receptor BP using [11C]raclopride, and measures of regional cerebral glucose metabolism (rCMRglc) after cocaine cue-exposure using [18F] -fluorodeoxyglucose (FDG) in PET .
Results: Treatment with modafinil resulted in 9.5% reduction in D2 receptor BP in the striatum, whereas treatment with topiramate resulted in 11% increase in D2 receptor BP in the striatum. Furthermore, modafinil reduced overall subjective measures of craving after treatment compared with pre-treatment measures, whereas treatment with topiramate had not effected craving measures. There were no effects of either medication on cue-induced craving before or after treatment.
Conclusions: Modafinil reduced measures of D2 BP in the striatum in patients concurrently dependent on cocaine and heroin, indicating increases in extracellular dopamine. This preliminary evidence will be discussed in view of the relative efficacy of these two promising medications in treatment for cocaine. Limitations include lack of total compliance with medication and, low rates of abstinence during treatment.
Financial Support: The Sakra-Rashi Trust in Paris France and Israel.

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DOES EARLY RESPONSE TO BUPRENORPHINE-NALOXONE PREDICT TREATMENT OUTCOME IN PRESCRIPTION OPIOID DEPENDENCE?

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Aims: The 10-site Prescription Opioid Addiction Treatment Study, conducted in the NIDA Clinical Trials Network, examined different lengths of buprenorphine-naloxone (bup-nx) plus medical management, with or without additional counseling, for patients dependent upon prescription opioids. Among patients (N=360) receiving 12 weeks of bup-nx stabilization, 49% achieved successful opioid use outcomes at week 12. The aim of this secondary analysis is to examine the ability to predict outcome (and thus potentially alter the treatment) based on early (weeks 1-4) treatment response.
Methods: Outcome was defined in 2 ways: 1) success, as defined in the main outcome paper, i.e., abstinence in week 12 of Phase 2 (the last week of bup-nx stabilization) and ≥2 of the previous 3 weeks; or 2) a stricter definition, i.e., opioid abstinence in weeks 9-12. Positive and negative predictive values were calculated based on the degree to which opioid abstinence or use in weeks 1, 1-2, 1-3, and 1-4 predicted outcomes in weeks 9-12.
Results: Outcome was best predicted by response after 2 weeks of treatment. Abstinence in the first two weeks was moderately predictive of treatment success in weeks 9-12 (positive predictive value = 71%), while opioid use in both of the first two weeks strongly predicted unsuccessful outcome at the end of bup-nx stabilization (negative predictive value = 84%), especially when outcome was defined as complete abstinence from opioids in weeks 9-12 (94%). Predictive values in week 1 alone were of only moderate strength (63% positive predictive value for abstinence, 70% negative predictive value for use), and data from weeks 3 and 4 added little to the predictive power of the first two weeks.
Conclusions: Evaluation (including urine testing) during weeks 1 and 2 of bup-nx stabilization can assist in predicting individualized treatment course and need for increased intensity of treatment services.
Financial Support: NIDA grants U10DA015831, K24DA022288

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SOCIAL INTERACTION MAY REDUCE AMPHETAMINE REWARD IN MALE ADOLESCENT RATS BY ACTIVATING MESOCORTICOLIMBIC DOPAMINE SYSTEMS.

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Aims: One way to predict if an adolescent will initiate drug use is whether or not their peers use drugs. In animals, social facilitation of drug taking behavior is only beginning to be understood. Recent work indicated that adolescent rats raised in isolated conditions find social interactions to be highly rewarding, especially in males. In a recent study in our laboratory, we found that individually housed adolescent male rats showed a conditioned place preference (CPP) for a compartment paired previously with a social partner. This social reward reduced amphetamine reward when rats were allowed choice between a social- and drug paired compartment concurrently. The current experiment tested the hypothesis that social interaction may compete with amphetamine reward by activating similar neural systems.
Methods: Male adolescent Sprague Dawley rats (28 days of age, n=16) were habituated to a CPP apparatus chamber for 30 min on the first session. The next session, half of the subjects were placed into a chamber alone for 30 min, while the other half were paired with a same-age male conspecific for 30 min. Immediately following the session, brains were dissected into medial prefrontal cortex (mPFC), dorsal striatum, nucleus accumbens (NAcc), and hypothalamus; brain levels of dopamine, DOPAC, 5-HT, and 5-HIAA were quantified by HPLC-EC.
Results: Results for dopamine utilization (DOPAC/DA) showed a main effect of brain region [$F(3,10)=88.957$, $p<0.001$] and a main effect of socialization [$F(1,12)=21.697$, $p=0.001$], with dopamine utilization elevated by social interaction across all regions. No significant effect of social interaction was observed with 5-HT utilization in any brain region examined.
Conclusions: These results indicate that social interaction activates mesocorticolimbic dopamine systems and that this neural activation may blunt the rewarding effect of amphetamine in adolescent male rats.
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CHOOSING MONEY OVER DRUGS: THE UNDERPINNINGS OF RATIONAL CHOICE IN COCAINE ADDICTS.

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Aims: There is a tension between the idea of damaged decision-making systems in addicts and the observation that some choices are rational. Cocaine addiction is portrayed as the hijacking of valuation signals, such as those in the striatum, where addicts are driven to choose cocaine over non-drug alternatives. In a simple depiction of this claim, choices away from cocaine would not involve the striatum. Hence, our working hypothesis that choosing money over cocaine would not correlate with striatal activity but other reward-guided brain areas.
Methods: Fifty human controls (Ctrls) and cocaine addicts (CAs) were scanned with fMRI during four inter-temporal choice tasks. Whereas single-commodity tasks (i.e., money now vs. money later, MM; and cocaine now vs. cocaine later, CC) have been used extensively, cross-commodity tasks (i.e., money now vs. cocaine later, MC; and cocaine now vs. money later, CM) have recently been designed to capture real-world trade-offs in addicts. The proportion of now and later choices was isolated and examined. Brain function was compared between groups while viewing and submitting now and later choices.
Results: In single-commodity tasks, CAs made fewer future money choices than Ctrls (40% vs. 58%, P<.02) with no difference in future cocaine choices. In cross-commodity tasks, CAs made more cocaine choices (MC=35%; CM=50%) than Ctrls (MC=17%; CM=08%), however, a large portion of CAs choices was for money (MC=65% and CM=50%). Whole brain analyses (P<.005, FWE) showed CAs had greater striatal responses for viewing and submitting money over cocaine choices, compared to Ctrls, and the left lateral prefrontal cortex was greater for future money choices.
Conclusions: The striatum and lateral prefrontal cortex participate in cocaine addicts forgoing cocaine for a non-drug alternative. These results highlight flexibility in addicts and provide context and targets for shifting choices from cocaine.
Financial Support: Supported by NIDA grants R01DA030241; R01DA024080; R01DA012997

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EFFECTS OF CANNABIS AND CIGARETTE SMOKING ON GRAY MATTER VOLUME: A VOXEL-BASED MORPHOMETRY STUDY.

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Aims: Neuroimaging studies have provided evidence of gray matter volume differences in drug dependent individuals compared to healthy control groups; however, these studies may be confounded by differences between groups in cigarette dependence. To examine the effects of chronic cannabis use on gray matter volume and to control for the effects of cigarette smoking, this study examined differences in gray matter volume between demographically matched cannabis-dependent individuals, nicotine-dependent individuals, and healthy controls using optimized voxel-based morphometry.
Methods: High-resolution T1 structural scans were obtained from cannabis-dependent individuals (n=26), nicotine-dependent individuals (n=26), and healthy controls (n=26). Groups were matched on age, sex, and years of education. Structural scans were segmented and registered using DARTEL in SPM8. Whole-brain analyses were conducted in SPM8 using random field-based cluster-size testing and family-wise error rate correction for multiple comparisons. Age, sex, and total gray matter volume were included as covariates.
Results: Regional gray matter volume was greater among cannabis smokers in the right cerebellum than cigarette smokers. Cannabis smokers had less gray matter volume than controls in the orbitofrontal cortex. Cigarette smokers had less gray matter volume than controls in the thalamus and bilateral cerebellum.
Conclusions: Findings suggest that cannabis-dependent individuals differ from healthy controls in that they have greater gray matter volume in the cerebellum and less gray matter volume in a frontal brain region involved in drug craving and reward. Gray matter volume differences between cigarette smokers and controls are consistent with previous research indicating significant effects of smoking on the thalamus and cerebellum. Future studies will examine whether these differences are associated with drug-motivated behaviors.
Financial Support: This work was supported by NIDA: R01 DA02845, R01 DA030394, and the Commonwealth of Pennsylvania CURE Addiction Center of Excellence Project.

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AGE EFFECTS IN METHYLPHENIDATE-INDUCED TASTE AVOIDANCE AND BDNF/TRKB ACTIVITY IN THE INSULAR CORTEX.

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Aims: Adolescents exhibit a shift in affective response to abusable drugs toward reward, which may ultimately lead to increased use. Drug intake is also influenced by dissociable aversive effects, which limit it, and both affective properties must inform assessments of drug risk. Recent work shows that adolescents are also protected from the aversive effects of many drugs as measured by conditioned taste avoidance (CTA). However, such effects of methylphenidate (MPH, widely prescribed to adolescents with ADHD) have not been characterized. Also, biochemical factors influencing CTA age effects are unknown, but could relate to BDNF activity in the insular cortex (IC), known to be central to CTA. Thus, we assessed MPH CTA in adolescent and adult rats with variations in IC BDNF activity. We predicted that adolescents would exhibit blunted CTA compared to adults, which would correlate with decreased BDNF activity.
Methods: MPH CTA was assessed in adolescent (PND 28-34, n = 34) and adult (PND 70-90, n = 33) male Sprague Dawley rats conditioned to four doses: 0, 10, 18 or 32 mg/kg, IP. Following, brain tissue was probed for IC BDNF and one of its target receptors, TrkB, as well as its activated form, p-TrkB, using Western blots. Data were analyzed with ANOVAs followed by tests of simple effects as appropriate.
Results: Expression of MPH CTA was blunted in adolescents versus adults, such that the former were slower to acquire avoidance and drank a higher percentage of saccharin than their adult counterparts in the CTA test (except at the 18 mg/kg dose). These results correlated with decreased activation of TrkB receptors in the IC, but a lack of drug effects within age groups suggests that it is not a general mechanism for CTA age effects.
Conclusions: As with many other drugs, adolescents are protected from the aversive effects of MPH, although the precise mechanism remains unclear, suggesting that abuse liability of MPH may be higher in this population.
Financial Support: Mellon Foundation to ALR and Dean's Research Grant to BBW.

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KNOWLEDGE ABOUT THE TRANSMISSION OF HIV AND HCV: A COMPARISON BETWEEN INJECTION DRUG USERS AND NON-INJECTION DRUG USERS.

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Aims: The purpose of this study was to examine the differences in knowledge about the transmission of HIV and HCV between injection drug users (IDUs) and non-injection drug users (NDUs). Transmission knowledge includes bodily functions and behaviors involving sexual interaction, drug use, and everyday contact. Demographic factors were also assessed.
Methods: A secondary data analysis of men and women (N = 324; M age = 41.6, SD=10.1) enrolled in a NIDA-funded NEURO-HIV Epidemiologic study in Baltimore, Maryland. Participants, recruited via street outreach, advertisements, and participant referral, completed a face-to-face psychosocial interview, including questions about demographics, drug use, and sex history. IDUs were operationalized as ever having used IV drugs and NDUs as never having used IV drugs.
Results: Both IDUs and NDUs displayed higher HIV knowledge than HCV transmission knowledge for all domains, which included drug use, bodily fluids, and physical contact. IDUs gave correct answers to HCV transmission questions significantly more often than did NDUs, particularly in the drug use domain: sharing needles, $\chi^2(3, N=324)=16.21$, $p=.001$; sharing cookers, $\chi^2(3, N=324)=19.12$, $p<.001$; sharing cotton, $\chi^2(3, N=324)=28.75$, $p<.001$; sharing rinse water, $\chi^2(3, N=324)=21.66$, $p<.001$; and backloading, $\chi^2(3, N=324)=30.82$, $p<.001$.
Conclusions: While HIV knowledge was higher than HCV knowledge in both groups, IDUs knew more about HCV transmission than NDUs. This demonstrates a knowledge gap in NDUs about the transmission of HCV. These findings indicate that NDUs represent a vulnerable population at-risk for HCV that lacks critical knowledge about HCV transmission.
Financial Support: This research was funded by NIDA R01 DA14498.

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EXAMINATION OF A RECOMMENDED ALGORITHM FOR ELIMINATING NONSYSTEMATIC DELAY DISCOUNTING DATA.

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Aims: Examine whether the use of a recommended algorithm (Johnson & Bickel, 2008) or a conventional statistical method (R2 <0 or missing) for identifying nonsystematic data in delay discounting (DD) data has a meaningful effect on research outcomes.
Methods: DD data were collected from 349 pregnant smokers (231 continuing smokers and 118 quitters) via a computerized task that compared $1000 at seven future time points with smaller values available immediately. Relationships between DD and smoking status were analyzed with and without the cases that met exclusion criteria based on the algorithm and conventional method (R2 <0 or missing) to evaluate the predictive utility of each. Multiple regression was used to classify participants with nonsystematic data.
Results: Nonsystematic responses on the DD task comprised a relatively large proportion of our data set (14-16%). Neither the algorithm nor the R2 method changed the relationship between discounting and important outcome measures, including predicting the smoking status of study participants. The algorithm excluded less data than the R2 method and unlike R2 it was not correlated with log k. Low educational attainment predicted nonsystematic DD data.
Conclusions: The algorithm shows some improvement over R2, by not being correlated with log k and eliminating fewer cases; however, there was no evidence that eliminating nonsystematic responding via either method significantly influenced the outcome of the results. Participants with lower educational attainment are more likely to produce nonsystematic data, suggesting potential merit in employing additional DD training when working with disadvantaged populations.
Financial Support: COBRE award P20GM103644 (NIGMS), TCORS award P50DA036114 (NIDA), R01DA14028 grant (NIDA), R01HD075669 grant (NICHD), T32DA07242 training grant (NIDA).

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PREVALENCE AND CORRELATES OF PRESCRIPTION STIMULANT MISUSE AMONG YOUTH IN THE EMERGENCY DEPARTMENT.

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Aims: Prescription stimulant misuse (PSM) is an important public health concern. The aims of this study are to determine the prevalence and correlates of PSM among youth seeking care in the Emergency Department (ED).
Methods: Possible participants 14-20 years old presenting to the ED at the University of Michigan Medical Center from 9/2010-3/2013 were systematically recruited as part of a larger trial. Participants completed a computerized self-report survey including past-year PSM defined as 'using prescription stimulants to get high, taking them when prescribed to someone else or taking more than prescribed'. Additional validated survey measures included substance use (i.e. ASSIST and AUDIT), previous injury and dating violence and a retrospective chart review was performed. A multinomial logistic regression analysis was used to compare those without PSM to those with mild risk PSM (ASSIST < 4) and those with moderate risk PSM (ASSIST ≤4).
Results: Of the 4389 participants (86.1% response rate; 57.9% were female; average age 17.5 years) 365 (8.3%) reported past year PSM. Among those with PSM, the majority (72%) reported PSM in the past 3-months and nearly one-third (32%) reported monthly, weekly or daily PSM. Additionally, 189 (51.7%) were mild risk and 176 (48.3%) were moderate risk as measured by the ASSIST. After controlling for age, gender, race, public assistance and academic performance, as compared to no past year PSM, correlates of mild risk PSM include other substance use, alcohol misuse and Caucasian race; correlates of moderate to high risk PSM were identical with the addition of past year dating violence.
Conclusions: Among youth in the ED, 8% report PSM with nearly 1/3rd of those reporting frequent PSM. ED-based screening and intervention efforts should consider PSM concomitant with alcohol and other drug use. Additionally, future studies should explore the association of dating violence with PSM and interventions should consider addressing both risk behaviors.
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ONLINE ATTENTIONAL RE-TRAINING FOR SMOKING.

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Aims: In previous studies, we found that computerized cognitive training was successful in changing cognitive biases for alcohol in alcohol-dependent patients, with positive effects on clinical outcomes (Schoenmakers et al., 2010; Wiers et al, 2011; Eberl et al., 2013). Given the computerized nature of these interventions, we now conducted several trials of online-only training. I will present results of online training for smoking cessation (and, in case of oral presentation, also for alcohol).
Methods: 425 smokers who wanted to quit were randomly assigned either to the experimental condition in which they were trained to avoid smoking cues during six sessions (visual probe test-based attentional re-training, cf. Schoenmakers et al. 2010) or to a continued assessment control.
Results: Attentional re-training proved effective in heavy smokers (15+ cigarettes a day), with no effect in light to moderate smokers (6-15 cigarettes per day). In heavy smokers attentional bias for smoking-cues tended to decrease more in the experimental group than in the control group. Moreover, in heavy smokers, abstinence of smoking was significantly higher in the experimental group (50%) than in the control group (23%). Attentional re-training did not change the approach-bias for cigarette simuli, a finding in line with recent findings in alcohol (specificity of attentional and approach bias).
Conclusions: These positive findings for the possibility of online attentional re-training to stop smoking in motivated smokers are important both for theoretical and for practical reasons. Theoretically it is important that positive results generalize from alcohol to smoking and also in an online-only format, because in anxiety positive findings in clinical samples were followed by negative results for online-only training. The practical implication is that an inexpensive online training module can help heavy smokers to quit smoking.
Financial Support: This study was made possible by a grant from the Dutch Medical Research Foundation (ZONMW). We declare no possible conflicts of interest.

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TARGETING THE SEROTONIN (5-HT) 5-HT$_{2C}$ RECEPTOR: RATIONAL DESIGN OF SMALL MOLECULE ALLOSTERIC MODULATORS TO TREAT PSYCHOSTIMULANT USE DISORDERS.

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Aims: Allosteric modulation of G protein-coupled receptors presents a promising approach to selectively target highly homologous receptor subtypes in a site- and event-specific manner conferring several benefits over the traditional targeting of orthosteric binding sites including reduced side-effect profile. Precisely, modulation of the serotonin (5-HT) 5-HT$_{2C}$ receptor (5-HT$_{2C}$R) is a novel approach with the potential to generate clinically-relevant compounds to treat psychostimulant use disorders. Based upon our recently identified 5-HT$_{2C}$R positive allosteric modulators (PAMs), we will optimize structural features and synthesize novel drug-like small molecules with high potency and selectivity for the 5-HT$_{2C}$R.
Methods: Utilizing a drug development team comprised of chemists and biologists, a series of new small molecules have been rationally designed, chemically synthesized, and pharmacologically characterized by using developed lead small molecules as templates, homology modeling and molecular docking techniques, as well as a battery of in-house *in vitro* (functional and radioligand binding studies) and *in vivo* (behavioral studies) assays to assess allosteric modulation of the 5-HT$_{2C}$R.
Results: To date, a series of new analogues have been designed and synthesized. Several advanced compounds have been identified to enhance 5-HT$_{2C}$R-mediated signaling events, including intracellular calcium (Ca_i^{++}). Additionally, molecular docking has been employed as a tool to provide the necessary information to design novel bitopic allosteric/orthosteric ligands which represent a unique strategy to develop novel chemical entities with anticipated enhanced binding affinity and specificity.
Conclusions: The design and synthesis of new 5-HT$_{2C}$R PAMs open new avenues in probing 5-HT$_{2C}$R function and discovering novel pharmacotherapeutics for psychostimulant use disorders.
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OPIOID OVERDOSE RISK PERCEPTION AND NALOXONE ACCEPTABILITY AMONG PATIENTS MAINTAINED ON CHRONICALLY PRESCRIBED OPIOIDS AT THE CINCINNATI VA.

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Aims: Among veterans receiving chronically prescribed opioids from the Opioid Substitution Clinic (OSC) or the Pain Management Clinic (PMC), determine: (1) knowledge of opioid overdose risk factors, (2) awareness of risk for overdose, and (3) acceptability of naloxone rescue kits.
Methods: We administered questionnaires to 100 veterans prescribed opioid medication for the past 3 months by a medical provider in the OSC or PMC. Questionnaire topics included demographics, over- or under- use of medications, use of substances, knowledge of opioid overdose, past experiences with opioid overdose, and knowledge of naloxone. We also reviewed veteran charts for opioid and sedative prescriptions for the past 3 months.
Results: The average dose of morphine-equivalent opioid prescribed was significantly higher in the OSC group, although the average dose reported taken by the PMC group was double that prescribed on chart review. More than half of veterans reported witnessing at least one opioid overdose, with an average number of 4 overdoses witnessed in both groups. About half OSC veterans reported experiencing an overdose compared to about one third PMC veterans. The average score on a test of opioid overdose risk factors was similar for both groups. The majority of both groups identified themselves as having a lower risk of opioid overdose than the average American. About 75% of both groups stated they would want a naloxone rescue kit if it were available.
Conclusions: Differences between veterans in OSC and PMC groups were less than expected. Veterans in both clinics were highly aware of some risk factors for overdose but not others. Although veterans in both clinics had substantial personal experience with overdose, most believed their risk for opioid overdose was lower than the average American adult. Veterans in both groups expressed a high interest in naloxone kits to treat overdose.
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CHARACTERISTICS OF POLY-SUBSTANCE USERS ENGAGING IN HIGH HIV-RISK BEHAVIORS.

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Aims: Drug use is associated with increased risk for HIV infection and transmission. This study hypothesizes differences in drug use history and current substance use between those engaging in HIV related high-risk versus low-risk behaviors, and aims to determine characteristics of poly-substance users engaging in high-risk HIV activities.
Methods: Data were analyzed from 157 out of treatment cocaine/heroin users (105 male, 52 female) who underwent screening for experimental laboratory studies. Participants completed the Risk Assessment Battery (RAB) and questionnaire measures of lifetime and current substance use behavior.
Results: The sample was divided into quartiles based on RAB total score to create low- and high-risk groups (*ns* = 44 and 38). Chi-square and *t*-tests indicated that the extreme quartile groups significantly ($p < .05$) differed in gender, $\chi2(1) = 5.56$, race, $\chi2(1) = 10.33$, and age, $t(78) = -2.34$, such that those in the high HIV-risk behavior group were more likely to be white, female, and younger. Individuals in the high-risk group reported significantly earlier ages of first cocaine use, $t(77) = -2.42$, and regular cocaine use, $t(76) = -2.16$, but not earlier ages of first heroin use, $t(56) = -1.15$, $p > .05$ or regular heroin use $t(55) = 0.50$, $p > .05$. The extreme quartiles did not significantly differ in total (quantity X frequency) past-month use of cocaine, $t(77) = -1.27$, or heroin, $t(77) = -1.93$. Extreme quartile groups did not differ in any (presence/absence) past month use of alcohol, $\chi2(1) = 0.22$, or marijuana, $\chi2(1) = 0.87$, however the high HIV-risk behavior group reported significantly higher rates of non-medical opioid use than the low-risk group, $\chi2(1) = 4.87$ (66.7% vs. 33.3%).
Conclusions: The results suggest demographic and drug use differences between cocaine/heroin users engaging in high versus low HIV-risk behaviors. The findings may be used to help identify individuals who could benefit from education regarding HIV transmission.
Financial Support: NIH R01 DA015462 and Joe Young, Sr./Helene Lycacki Funds (State of Michigan)

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AN INTERNET-ACQUIRED RECOVERY SAMPLE: INITIAL FINDINGS FROM THE INTERNATIONAL QUIT AND RECOVERY REGISTRY.

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Aims: Recovery is an important process in the addiction life-cycle. As such, recovery has been previously studied using either 1) longitudinal designs, or 2) large generally cross-sectional samples. Both approaches may incur large financial and labor burdens. However, internet-based methods have the potential to integrate these approaches while minimizing the challenges of these other methods. Here, we report the initial findings from The International Quit and Recovery Registry, which is a tool we are using to characterize formally addicted individuals using these methods.
Methods: To register, an individual had to submit an active and unregistered email address to the website (https://quitandrecovery.org/) and click on a link that was emailed to the individual so that they could fill out a registration questionnaire. Respondents who 1) did not report a primary addiction or 2) were less than 18 years old at the time of registration were excluded from data analyses.
Results: 3063 individuals registered (53.7% female) with an average age of 47.8 (SD = 12.2). The median number of years in recovery is 5.1 years (with an IQR of 11.8 years), and 35% of this sample report being in recovery for three years or less. The most common primary addiction reported is alcoholism (51.7%), and the broadly classified "inpatient therapy" (54% of 2536 respondents) is reported as the most effective treatment method. 96% of registrants report having at least one secondary addiction.
Conclusions: This registry allowed for the study of a large and diverse sample of individuals in either initial or long-term recovery. Future follow-up studies will determine whether longitudinal study is possible through this method, as well as characterize the recovery phenotype.
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SEX DIFFERENCES IN COGNITIVE AND MOTOR IMPULSIVITY AMONG USERS OF DIFFERENT CLASSES OF DRUGS IN PROTRACTED ABSTINENCE.

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Aims: We examined sex differences in cognitive and motor impulsivity among heroin users (HU), amphetamine users (AU), and polysubstance users (PU) in protracted abstinence (>1 yr) and healthy controls (HC).
Methods: Participants (men = 230; women = 77) completed tasks of motor impulsivity (Go/No-go Task [GNGT]; Immediate Memory Task [IMT]) and cognitive impulsivity (Cambridge Gambling Task [CGT]; Iowa Gambling Task [IGT]; Delayed Reward Discounting Task [DRDT]). Drug users and HC were matched on IQ and education. ANCOVAs examined effects of sex and drug class on performance.
Results: Women demonstrated motor impulsivity deficits compared to men, evidenced by more errors of commission and omission and lower discriminability (d') on the GNGT. Female HU evidenced selectively impaired d' on the IMT. Women also demonstrated cognitive impulsivity deficits relative to men. On a task of decision-making under ambiguity (IGT), women performed disadvantageously, an effect driven by female PU. Women also performed disadvantageously on the CGT by betting lower amounts and failing to adjust bets based on explicit risk contingencies, which was also driven by female PU. Finally, both female HC and AU engaged in higher DRD than male HC and female HU.
Conclusions: Women demonstrated impulsivity, inattention, and reduced discriminability on tasks of motor impulsivity. On measures of cognitive impulsivity, women evidenced impaired decision-making and risk-taking. Specifically, women were disadvantageously risk-averse on a probabilistic decision-making task (CGT), while they demonstrated elevated risk-taking under ambiguity (IGT). Different classes of drugs were associated with distinct impairments: female HU demonstrated reduced ability to discriminate between targets and non-targets; female AU demonstrated higher discounting of delayed rewards; and female PU demonstrated risky decision-making when contingencies were ambiguous and risk-averse decision-making when contingencies were explicit.
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A MULTI-SITE, DOUBLE-BLIND, PLACEBO-CONTROLLED PILOT CLINICAL TRIAL TO EVALUATE THE EFFICACY OF BUSPIRONE AS A RELAPSE-PREVENTION TREATMENT FOR COCAINE DEPENDENCE.

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Aims: To evaluate the potential efficacy of buspirone as a relapse-prevention treatment for cocaine dependence.
Methods: A randomized, double-blind, placebo-controlled, 16-week pilot trial conducted at six clinical sites. Adults meeting DSM-IV-TR criteria for current cocaine dependence scheduled to be in inpatient/residential substance use disorder (SUD) treatment for 12-19 days when randomized, and planning to enroll in local outpatient treatment through the end of the active treatment phase were randomized to buspirone titrated to 60 mg/day (n=35) or to placebo (n=27). All participants received psychosocial treatment as usually provided by the SUD treatment programs in which they were enrolled. Outcome measures included maximum days of continuous cocaine abstinence (primary), proportion of cocaine use days, and days-to-first-cocaine-use during the outpatient treatment phase (study weeks 4-15) as assessed by self-report and urine drug screens.
Results: Study retention was high (94% completion rate) and medication adherence was strong (85% based on medication events monitoring system). There were no significant treatment effects on maximum continuous days of cocaine abstinence or days to first cocaine use. Buspirone, relative to placebo, significantly increased the proportion of cocaine use days ($X^2(1)=6.06$, p=.01), which reflected an effect in the female participants (n=23; $X^2(1)=15.26$, p<.0001), that was not detected in the male participants (n=39; $X^2(1)=0.14$, p=.70).
Conclusions: The results suggest that buspirone is unlikely to have a beneficial effect on preventing relapse to cocaine use and that buspirone for cocaine-dependent women may worsen their cocaine-use outcomes.
Financial Support: National Drug Abuse Treatment Clinical Trials Network (NIDA CTN)

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RISK FACTORS ASSOCIATED WITH OVERDOSE AMONG PATIENTS SEEKING TREATMENT FOR OPIOID DEPENDENCE.

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Aims: Drug overdose is the leading cause of injury death in the United States and patients in treatment for opioid dependence are at high risk of overdose. The purpose of this study is to identify overdose risk factors for patients in residential treatment for opioid dependence.
Methods: Analysis of data from an opioid overdose prevention program evaluation located in a metropolitan area in the midwest. This analysis includes baseline data from 86 residential patients that consented to study participation.
Results: The majority of subjects (78%) reported having either witnessed or experienced an overdose during their lifetime. The mean age of first overdose was 27.9 years old (SD=7.6) and 83.3% of those who reported having ever attempted suicide had also overdosed. Unadjusted factors associated with an increased odds of overdose include higher education, not working prior to entering treatment, ever prescribed a psychiatric medication, and number of times treated during lifetime in an emergency department. In the multivariable analysis, only not working prior to entering treatment remained statistically significant and a sensitivity analysis revealed that risk factors vary by gender.
Conclusions: Identification of overdose risk factors for patients seeking treatment for opioid dependence will help improve prevention interventions in these settings.
Financial Support: This research is supported by a grant from Interact for Health.

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CAN A BRIEF INTERVENTION BE EFFECTIVE FOR ADOLESCENTS WITH A SEVERE-END DRUG PROBLEM?

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Aims: Prior evaluations of a manually-guided brief intervention, Teen Intervene, have supported the program's efficacy (e.g., Winters et al., 2012; in press). This indicated preventive intervention is intended for adolescents with a mild-to-moderate drug abuse. Nonetheless, many study enrollees met criteria for a DSM-IV substance dependence disorder, or were classified as "diagnostic orphans" (1 or 2 dependence symptoms but no abuse symptoms). The aim of this submission is to examine the program's effectiveness for those youth with a more severe-end form of alcohol and marijuana involvement. We hypothesize that outcomes are less favorable among those youth with severe-end drug involvement.
Methods: We re-analyzed our alcohol and marijuana outcome data (6- and 12-months post-intervention) by examining outcome as a function of count of SUDS at baseline, separately for alcohol and marijuana. Outcome variables were alcohol/marijuana use frequency (4-point scale) and abstinence rates. A logistical regression analysis was used that controlled for gender and age.
Results: The SUDS count variables were modestly associated with outcome. Consistent with the hypothesis, outcomes at both 6 and 12 months were less favorable (more post-intervention drug use and lower abstinence rates) for those with the higher count of SUDS. The analysis organized around baseline DSM-5 criteria for a substance use disorder diagnosis also showed the same pattern of results (i.e., those with severe DSM-5 dx had worse outcomes compared to cases that met mild or moderate DSM-5 dx).
Conclusions: These findings further reinforce that brief interventions for youth may be best suited for those with a mild or moderate drug problem. Youth with several dependence symptoms may need more treatment than what is typically provided in a brief intervention.
Financial Support: Research supported by NIDA Grants R01-DA17492 and K24- DA035882.

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PREDICTORS OF SUBLINGUAL BUPRENORPHINE INDUCTION AND DETOXIFICATION RESPONSE AMONG HEROIN-DEPENDENT ADULTS.

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Aims: The present study investigated predictors of opioid abstinence (proxy for treatment success) in heroin-dependent adults during buprenorphine (BUP) induction and detoxification.
Methods: This retrospective analysis of four non-treatment research trials included adult (18-55 yr) heroin users. Inpatient experimental procedures varied across trials, but BUP induction, maintenance and detoxification procedures were identical. Heroin-dependent individuals (SCID and urinalysis verified) were stabilized on BUP 8mg/day for >10 outpatient days [induction] prior to each inpatient phase. Unsanctioned drug use was not permitted inpatient (urinalysis verified; 8mg/day BUP maintenance). After study completion, subjects were discharged and underwent outpatient BUP dose tapering [detoxification]: 4mg (wk 1) to 2mg (wk 2) to 0mg (wk 3) daily. Abstinence-contingent reinforcement [$30/consecutive opioid-free urine sample (M-W-F)] was used to discourage opioid lapse during detoxification. The modal subject (N=65) undergoing BUP induction was a 42 year old African American (54%) male (82%). Subjects (n=28) who completed the source experiments underwent BUP detoxification. Subject drug use characteristics were considered in regression models predicting opioid abstinence during BUP induction and detoxification.
Results: Logistic regression indicated being older at initial heroin use and fewer past-month days using heroin prior to induction accurately (78%) predicted subjects achieving any opioid abstinence during BUP induction [$F(2)=8.4$, p<.05]. More lifetime attempts to quit heroin (HQA) and any opioid abstinence during BUP induction accurately predicted (68%) which subjects maintained continuous opioid abstinence throughout active BUP dosing during detoxification [2 wks; $F(2)=5.8$, p=.05]. Linear regression indicated more HQA and higher % opioid-free urine samples during induction predicted longer time to lapse during BUP detoxification [r2= 23%, $F(2,27)=3.8$, p<.05].
Conclusions: Identifying accurate predictors of BUP response may improve clinical outcomes.
Financial Support: 1 NIH R01 DA015462 and Joe Young Sr./Helene Lycacki Funds (State of Michigan).

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RESIDENTIAL MOBILITY AND HOUSING INSTABILITY AMONG JUSTICE-INVOLVED AFRICAN-AMERICAN OPIOID ABUSERS.

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Aims: Social and economic supports are often fractured for justice-involved individuals, which impacts involvement in treatment. Little research assesses how housing status and residential transitions relate to substance use and criminal offending among justice-involved individuals.
Methods: The sample includes individuals screened for eligibility in a randomized clinical trial on buprenorphine (n=210). All clients were currently involved in the justice system (probation, parole, or pre-trial release services) and addicted to opioids within the prior 12-months of their assessment. OLS regression models with robust standard error were conducted to explore how the number of changes in housing status, residential mobility (living at home, relatives, or friend's residence), and residing at a halfway house or homeless shelter predict days of illicit substance use, alcohol consumed, and criminal activity.
Results: Those who were less residentially mobile (t=-3.63; p<.001) and spent more days stably housed (t=2.02; p<.05) were considerably more likely to self-report criminal activity. Residing at a halfway house or homeless shelter was associated with a lower likelihood of criminal activity (t=-2.08; p<.05). Participants who resided at halfway house or homeless shelter (t=1.79; p=.08) had a lower frequency of substance use. Housing factors were unrelated to alcohol use.
Conclusions: Participants who were less residentially mobile and more stably housed had a higher likelihood of criminal involvement. These findings were likely due to the participants' stronger social ties to those criminally-involved. Justice-involved individuals residing at a halfway house and homeless shelter was associated with a lower likelihood of illicit substance use and criminal activity, likely due to housing requirements that regulate behavior. Further research in this area needs to explore how social ties moderate the effects of housing stability and mobility on crime and substance use.
Financial Support: National Institute of Drug Abuse, NIDA R01 DA030768 (PI: Altice, Lawson, and Taxman).

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CHRONIC PAIN VOLATILITY PREDICTS OUTCOMES OF BUPRENORPHINE-NALOXONE FOR PRESCRIPTION OPIOID DEPENDENCE.

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Aims: Prescription opioid (PO) dependence frequently co-occurs with chronic pain. Prior studies did not find poorer buprenorphine-naloxone (BUP-NLX) outcomes in chronic pain patients, but more dynamic indicators of chronic pain may impact treatment. We hypothesized that greater pain volatility would predict opioid use during BUP-NLX taper in adults with PO dependence and chronic pain.
Methods: This secondary analysis of CTN POATS included the subset of participants with chronic pain who entered Phase II and started BUP-NLX taper (N = 113). Dynamic indicators of pain included person-specific intercepts, slopes, and volatility (mean absolute deviation) obtained from mixed models of pain ratings during 12-week BUP-NLX stabilization. Prospective relations between pain indicators and urine-verified opioid use during the 4-week taper were examined using multilevel logistic regression, controlling for treatment condition as standard medical management (SMM) vs. SMM + opioid dependence counseling (SMM+ODC).
Results: Pain severity decreased during BUP-NLX stabilization (-.40, p < .001). Nearly 40% of the sample tested positive for opioids during the 4-week BUP-NLX taper. In multilevel logistic regression, greater pain volatility predicted greater odds of opioid use during BUP-NLX taper, (OR = 14.25, p < .01), controlling for SMM vs. SMM+ODC (OR = 8.11, p < .05) and pain change over time (OR = 3.54, p < .01).
Conclusions: Individuals with chronic pain and greater pain volatility during BUP-NLX maintenance are more likely to use opioids during BUP-NLX taper, independent of treatment group, initial pain, and change in pain. This finding suggests intra-individual pain volatility represents unique risk for continued opioid use. Attention to pain volatility may assist clinicians in optimizing treatment of co-occurring chronic pain and PO dependence, and future studies should examine underlying biological, psychosocial, or contextual factors related to pain volatility.
Financial Support: NIDA CTN and NIDA 5T32DA026400

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ALCOHOL DEPENDENCE, GENDER, AND CORTISOL RESPONSE PREDICT AMYGDALA RESPONSE PATTERN TO FMRI STRESS TASK.

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Aims: Lifetime prevalence rate of AD is 12.5% (Hasin et al., 2007). As a result of stress, neural dysfunction in frontolimbic regions including the amygdala has been noted in healthy individuals (Lovallo, 2012) and serves as a risk factor in AD (Koob & Kreek, 2007). Gender moderates stress, with differences in stress response to stress and alcohol cues (Seo et al., 2011). This study examines the effects of AD and gender on stress response in the amygdala, and whether cortisol functioning predicts amygdala response.
Methods: Data were collected from 10 abstinent AD (6 female) and 11 controls (6 female). Subjects participated in an fMRI stress task based on the Trier Social Stress Task. Multiple regressions were run to examine if AD group status, gender, or AD*gender predicted amygdala pattern of response (measured by area under the curve, AUC). Follow up analyses in AD were conducted to examine if cortisol levels collected a year prior to the scan prospectively predicted amygdala activation.
Results: Controlling for gender and handedness, AD group predicted left and right initial and total (ps<.001) amygdala activation. Gender differences in left amygdala also existed, with females exhibiting greater left initial and sustained (ps<.03) activity. Controlling for gender, increased cortisol stress response measured a year prior to the scan predicted increased left amygdala initial response (p<.05) and marginally predicted left sustained (p<.07), right initial and sustained (ps<.09) amygdala activation.
Conclusions: The current study found that AD predicted amygdala response in an fMRI stress task; the AD group showed elevated amygdala activation. Gender predicted left amygdala activation, with females having increased activation. AD status did not interact with gender. In AD, cortisol measured in a hormone challenge task a year prior to the scan predicted amygdala activation. Implications will be discussed.
Financial Support: UC URC Interdisciplinary Grant PIs: Medina & Anthenelli 3R01DA030354 PI: Lisdahl

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DIFFERENT DYNAMIC RELATIONSHIP BETWEEN STRESS AND ILLICIT DRUG USE FROM PREGNANCY TO POSTPARTUM AMONG DRUG-USING WOMEN.

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Aims: To document dynamic changes in the relationship between stress and illicit drug use from pre-pregnancy to post-partum
Methods: During a larger longitudinal (24-month) study of women's drug use, 49 women reported using drugs in the last 30 days at baseline and became pregnant during the course of the study. Self-reported drug use and perceived stress were examined at 4 months pre-pregnancy, during each trimester, and 6 months postpartum.
Results: Drug-using pregnant women reported a general decline in perceived stress from pre-pregnancy through pregnancy, with varying levels of perceived stress from delivery to 6 months postpartum. Drug use declined sharply from pre-pregnancy through the 3rd trimester, and then increased during postpartum. Dynamic coupling modeling revealed distinct temporal relationships between perceived stress and drug use during pregnancy from postpartum. During pregnancy, we observed a reciprocal relationship between stress and drug use from 2 months prior to 2nd trimester but not in 3rd trimester. Postpartum, although drug use predicted subsequent changes in drug use, perceived stress did not predict subsequent drug use until 6 months postpartum.
Conclusions: Among drug using women, pregnancy appears to change the dynamic between stress and drug use. This may partially explain the inconsistent reports of relationship between stress and illicit drug use in pregnancy and postpartum among high risk groups of women, depending on when the data are collected.
Financial Support: This research was in part funded by the National Institutes of Health, National Institute of Drug Abuse, R01DA020058 and K01DA021814 awarded to Zhao Helen Wu.

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AREA-LEVEL ATTRIBUTES AND PROGRAM RESOURCES AS PREDICTORS OF METHADONE DOSAGE PATTERNS.

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Aims: Organizational and client characteristics have been shown to be associated with differences in methadone dosages administered by outpatient substance abuse treatment programs. However, there is a dearth of research on the role of area-level attributes (county-level) in determining resource availability and treatment practice. We examine the role of areal-level demographics, economic characteristics, program structural characteristics and resources in determining patterns in methadone dosages.
Methods: Structural equation modeling is used to estimate causal relationships between county characteristics and program resources, and the relationship between dosage and program resources and characteristics. Program data come from the 1990 – 2011 National Drug Abuse Treatment System Survey (NDATSS), and includes a sample of 702 programs. Area-level data were collected from the American Community Survey and the Area Health Resources Files. Methadone dosage rates were measured by percentage of patients receiving dosages below 40, 60 and 80 mg/day.
Results: County density and median income were positively associated with methadone program income; median county income formed a positive relationship with expenditures per patient, after controlling for program income and total patients. Patient methadone dosage levels were significantly related to a county's unemployment rate and median income. High county population density is associated with lower methadone dosages. However, increased county unemployment rates and program income were found to be associated with increased rates of patients receiving higher dosages, controlling for total number of clients.
Conclusions: Area-level attributes and program resources are important determinants of variation in program treatment practices. The significant relationship between these factors and concentrated racial and ethnic populations may be significant contributors in predicting the likelihood of patients receiving recommended dosage levels. Future studies should define causal pathways and specify the effects of area-level characteristics on program resources and treatment.
Financial Support: KL2 TR000081, R01DA030459

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RISK OF STARTING TO SMOKE TOBACCO CIGARETTES IN THE UNITED STATES: ESTIMATES FOR FOREIGN-BORN VS. U.S.-BORN YOUNG PEOPLE, 2002-2009.

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Aims: In the USA, the risk of starting to smoke tobacco is found to vary across US-born and foreign-born (FB) young people and across family heritage subgroups. In this project, we aim to shed new light on how environmental influences might shape these variations by taking into account elapsed time from immigration to smoking onset.
Methods: Study estimates are based on U.S. National Surveys of Drug Use and Health (RDAS, 2002-2009), each with a nationally representative sample of non-institutionalized civilians age 12 years and older (n>50,000 each year), and IRB-approved computerized self-interviews on smoking, nativity, family heritage, and years lived in the US. Weighted data with complex survey variance estimation yield values reported below.
Results: Among US-born youths, an estimated 7.4% start to smoke each year (95% CI = 7.2%, 7.6%). For FB youth living in the US < 5 years, 5-10 years, and >10 years, the risk estimates show a pattern toward convergence with USB estimates: 4.2% (95% CI =3.6%, 4.9%); 4.6% (3.8%, 5.5%); 6.9% (6%, 7.9%), respectively (test for trend, $p < 0.05$). However, patterns vary by family heritage. For example, estimated risk of starting to smoke for foreign-born non-Hispanic Blacks is uniformly lower, irrespective of time in the US. For some Asian-American subgroups, the risk estimates often exceed those of US-born youths.
Conclusions: The health of new US immigrants is an important topic, and this evidence discloses dynamic environmental influences against a background of more stable family-genetic and home country risk determinants. We hope this line of research eventually might help to shape more appropriately targeted prevention and early intervention programs for foreign-born young people, as well as their US-born peers.
Financial Support: NIDA T32DA021129 (WVX); MSU (CLQ); K05DA015799 (JCA).

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TEMPORAL PROFILE OF FRONTO-STRIATAL-LIMBIC ACTIVITY DURING IMPLICIT DECISIONS IN DRUG DEPENDENCE.

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Aims: Substance dependence is associated with impaired decision-making and altered fronto-striatal-limbic activity. Both increases and decreases in brain activity have been reported in drug users compared to controls during decision-making. Inconsistent results might be explained by group differences in the temporal profile of the fMRI response. While prior studies have analyzed data assuming a canonical hemodynamic response profile, a finite impulse response (FIR) model measures the fMRI signal at discrete time points without assuming any particular temporal profile. We compared brain activity during decision-making and feedback in substance users and controls using two models: a canonical hemodynamic response function (HRF) and a FIR model.
Methods: 37 substance-dependent individuals (SDI) and 43 controls performed an event-related decision-making task during fMRI scanning. Brain activity was compared across group using canonical HRF and FIR models.
Results: SDI were impaired at decision-making compared to controls. The canonical model showed that SDI had increased fronto-striatal-limbic activity during decisions and decreased activity during feedback. FIR analysis confirmed increased activity in SDI during decisions. However, "decreased" activity in SDI during feedback corresponded to a lower post-stimulus undershoot of the hemodynamic response.
Conclusions: Increased activity in fronto-striatal-limbic pathways in SDI compared to controls is consistent with prior work further supporting the hypothesis that abnormalities in these circuits underlie impaired decision-making. We demonstrate for the first time using a FIR analysis that "reduced" activity during feedback may simply reflect the tail end of the response to decision, the post-stimulus undershoot, rather than an actual difference in response to feedback.
Financial Support: National Institute of Drug Abuse DA024104 and DA027748

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FEMALE OPIOID USERS MAY BE AT EXCESS RISK OF BECOMING DEPENDENT SOON AFTER EXTRA-MEDICAL PRESCRIPTION PAIN RELIEVER USE IN ADOLESCENCE BUT NOT IN YOUNG ADULTHOOD: ESTIMATES FOR THE UNITED STATES, 2002-2011.

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Aims: Here, we aim to estimate male-female differences in a rapid transition to a dependence syndrome, once there is occurrence of the first extra-medical use of prescription pain relievers (e.g., to get high, EMPPR). We also seek to shed light on variations for adolescent-onset versus later-onset EM users, as well as time trends in this transition probability.
Methods: Nationally representative sample data from more than 28,000 EMPPR users come from U.S. National Surveys on Drug Use and Health (NSDUH, 2002-2011), with an IRB-approved protocol that involved computerized self-interview assessments of the study variables. Newly incident users initiated EMPPR use < 24 months before assessment. Analysis-weighted estimation yields Taylor series variances for complex survey data.
Results: Among females, an estimated 7% of adolescent-onset EMPPR users had become dependent, vs. 4% among male newly incident users ($p<0.05$), with no male-female difference seen among later-onset EMPPR users ($p>0.05$). Analyses of subgroup variation disclosed a possibly increasing time-trend in risk of dependence among newly incident EMPPR users.
Conclusions: Building from Seedall & Anthony (2013) and Parker & Anthony (under review), we find some evidence that adolescent EMPPR users are more likely make a rapid transition and to become dependent, but this is not the case when EMPPR use starts in young adulthood. Underlying sex-associated neurobiological and neuropsychopharmacological mechanisms deserve more attention as we seek to understand these developmental risk variations.
Financial Support: MSU research funds (HH) and NIDA K05DA015799 (JCA)

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NEURAL FUNCTION AND STRUCTURE AMONG YOUNG MEN WITH CANNABIS DEPENDENCE: RELATIONSHIP TO TREATMENT RESPONSE.

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Aims: Cannabis remains one of the most widely abused drugs worldwide yet the efficacy of current treatment options for cannabis dependence (CBD) remains limited. Structural and functional MRI may help identify biological factors related to treatment response.
Methods: Twenty men with cannabis dependence (CBD) were recruited from a randomized clinical trial of behavioral treatments and participated in pretreatment neuroimaging of the Monetary Incentive Delay task, along with 20 age- and gender-matched healthy comparison (HC) participants. Structural and functional MRI data analyses focusing on the striatum were used to compare CBD and HC participants. CBD participants were further divided based on subsequent attainment of three or more weeks of consecutive abstinence during treatment in order to explore any differences in brain structure or function between treatment responders and non-responders in relation to HC participants.
Results: CBD participants had significantly increased right ventral striatal (VS) activity (t=3.2, pFWE=.03) during the receipt of monetary rewards (outcome phase) and significantly smaller putamenal volumes (R: F=4.7, p=.04; L: F=6.8, p=.01), compared to HCs. In comparison to HCs, CBDs who subsequently achieved ≥3 weeks of abstinence had significantly greater right VS activation (F=15.6, p=.001) pre-treatment. In contrast, CBDs who did not achieve three week abstinence had significantly smaller putamenal volumes pre-treatment (R: F=6.0, p=.02; L: F=7.1, p=.04) compared to HCs, but did not significantly differ from HCs on functional MRI measures.
Conclusions: Men with CBD exhibit functional and structural differences within the striatum prior to behavioral treatment interventions, compared to gender- and age-matched HCs. Findings from exploratory comparisons of CBD subgroups indicate that differences in brain function and structure may relate to the subsequent achievement of abstinence in response to such interventions, and therefore may be useful in guiding treatment interventions in the future.
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DETECTING A SIGNAL IN THE NOISE: RESULTS OF A PILOT PROJECT TO MONITOR THE GLOBAL SPREAD OF NEW DRUGS BY MONITORING MEDIA.

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Aims: Monitoring use of, and harms associated with, Novel Psychoactive Substances (NPS) (i.e., synthetic/designer drugs) poses a number of considerable challenges. Estimates of prevalence are problematic and it is currently not possible to make international comparisons. The objective of the current study was to determine the feasibility and utility of using media reports and other open source information collected by the Global Public Health Information Network (GPHIN) to monitor the global spread of NPS. To this end we examined English media reports on synthetic cannabinoids from 1997 to the 2013.
Methods: GPHIN is an event-based surveillance system operated by the government of Canada and the World Health Organization (WHO) that uses media to monitor the global spread of infectious diseases. Media reports collected by the GPHIN between 1997 and 2013 were searched for reference to synthetic cannabinoids. The resulting reports were screened for relevance and the location, and nature of the media reports (i.e., report of morbidity, arrest, etc.) were extracted and plotted geographically and over time.
Results: The pattern of results very closely resembled other indicators of synthetic cannabinoid use. When plotted over time, the number of media reports from the U.S. resembled the number of U.S. poison control center exposures.
Conclusions: Media monitoring has great promise in accurately tracking the emergence and spread of NPS. We suggest a media monitoring system such as this would be highly complementary to current national and international monitoring efforts and, given the work already conducted by GPHIN, would require relatively little investment of resources to establish and operate.
Financial Support: Health Canada

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INDIVIDUALIZED TREATMENT FOR TOBACCO DEPENDENCE IN ADDICTIONS TREATMENT SETTINGS: THE ROLE OF CURRENT DEPRESSIVE SYMPTOMS ON OUTCOMES AT 3- AND 6-MONTHS.

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Aims: Individuals with concurrent tobacco dependence and other addictions often report depressive symptoms and as such may have more difficulty quitting smoking. We hypothesized that current symptoms of depression would be a significant predictor of quit success among a group of smokers receiving individualized treatment for tobacco dependence within addiction treatment settings.
Methods: Individuals in treatment for other addictions were enrolled in a smoking cessation program involving brief behavioural counseling and individualized dosing of nicotine replacement therapy. The baseline assessment included the PHQ9 for depression. Smoking cessation outcomes were measured at 3 and 6 months post enrollment. Bivariate associations between cessation outcomes and PHQ9 score were analyzed.
Results: Of the 919 subjects enrolled to date, 817 (89%) completed the entire PHQ9. Anhedonia was endorsed by 50.7% of the sample. Moderate to severe depression (score >9) was reported by 27.5% of the sample, and another 27.9% reported mild depression (score between 5 and 9). There were significant gender differences in both depression scores and cessation outcomes so gender was entered as a covariate in the analysis. Contrary to the extant literature and other findings by our own group, there was no association between current depression and cessation outcome at either 3-months (n=429) (25.9% vs 28.4%, p=0.55) or 6-months (n=282) (33.5% vs 31.4%, p=0.7).
Conclusions: Contrary to our hypothesis, depression severity did not predict cessation outcome in this study. A possible explanation may be the individualized treatment and supportive environment of an addictions treatment setting. These data indicate that patients in an addictions treatment setting can successfully quit smoking regardless of current depressive symptoms.
Financial Support: The research was funded by the Ontario Ministry of Health and Long Term Care - Health Promotion Branch.

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COMPARISON OF IMPULSIVITY AND DECISION MAKING IN KETAMINE, OPIOID AND NON-DRUG USERS.

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Aims: To test the hypothesis that ketamine users have impulsivity and decision making deficits similar to opioid users, by comparing impulsivity and decision making of adult ketamine users (KAU), engaged in methadone maintenance treatment (MMT), or healthy non-drug using controls (NDC).
Methods: Participants were recruited using advertisements and chain referral. A case–control observational design was used to compare the KAU (n = 23), MMT (n = 29), and NDC (n = 20) groups on impulsive personality (Barratt Impulsiveness Scale), response inhibition (Stroop Test, stop-signal test), working memory (2-back task), and decision making (Iowa gambling task IGT); we also measured the antisocial traits (Psychopathic Deviate scale in MMPI), and emotion state (Chinese Affect Scale and a self-report depression scale, CES-D). The groups were compared using one-way ANOVA, followed by planned post hoc pair-wise tests, and effect sizes were calculated using Cohen's d.
Results: KAU and MMT, as compared to NDC, had elevated BIS scores ($p < .05$) showed poorer performance on the 2-back working memory ($p < .01$) and stop-signal task ($p = .09$) tests, and were more likely to be in the clinically significant range on the MMPI Pd scale ($p < .05$). MMT had the highest stop-signal miss rates, whereas KAU had the lowest 2-back accuracy. There were no significant group differences in terms of cognitive performance on the IGT and Stroop Test.
Conclusions: Consistent with our hypothesis, ketamine and opioid users showed similar patterns of poor impulsivity and antisocial traits but not decision making. Impulsivity and antisocial personality may contribute to the persistence of ketamine or other drug use among KAU or MMT. Future treatments might benefit from addressing these shared risk factors for drug use disorders.
Financial Support: This work was funded by National Natural Science Foundation of China 31271113.

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PUBLICATION TRENDS FROM 1950–2009: OPIOIDS, BENZODIAZEPINES, BARBITURATES, AND AMPHETAMINES.

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Aims: To quantify and describe the trends in publications for opioids, benzodiazepines, barbiturates, and amphetamines over six decades.
Methods: A MEDLINE search for all publications (1950 – 2009) with MeSH terms "Analgesics, Opioid", "Benzodiazepines", "Barbiturates", and "Amphetamine" was conducted. A limit to "reviews" was also applied. The number of publications, reviews and growth rates were analyzed across consecutive decades.
Results: A total of 214,353 articles were found in the MEDLINE search. The number of publications on opioids (n=81,041) has grown consistently since the 1970s; averaging a 32% increase per decade from 1970-2009. The number of opioid publications peaked in the 2000s (n=26,667). Benzodiazepine publications (n=54,193) peaked in the 1990–1999 decade (n=15,401), with a dramatic slowing in the growth rate since the 1980s, and a steady increase in the proportion of review articles. The number of publications on barbiturates (n=49,315) peaked in the 1970s (n=15,257) and has been declining ever since. The number of publications on amphetamines (n=29,804) has increased steadily since the 1950s, with the exception of the 1980s. In recent years, amphetamine publications have had the fastest growth rate; a 45% increase from the 1990s to the 2000s.
Conclusions: Opioids had the largest number of publications over the 6 decades analyzed using the MEDLINE database, with substantial growth each decade. In contrast, although benzodiazepines had the second largest number of publications, there has not been substantial growth in the last 3 decades, and the proportion of reviews has increased. As expected, barbiturate publications have declined dramatically since the 1970s. Although smaller in number, publications on amphetamines have steadily increased. These findings are consistent with recent trends focusing on opioids amongst prescription drugs of abuse. Re-visiting benzodiazepine-related research needs may be warranted.
Financial Support: None

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OVEREXPRESSION OF ΔFOSB IN RAT NUCLEUS ACCUMBENS SHELL MIMICS ENVIRONMENTAL ENRICHMENT IN SUCROSE SELF-ADMINISTRATION AND COCAINE SEEKING.

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Aims: Previous research has shown that environmental enrichment produces protective addiction and depression phenotypes. In addition, rats reared in the enriched condition have a higher △FosB protein level than rats reared in isolated condition. However, the consequences of △FosB accumulation and its influence on sucrose and cocaine taking behaviors are not clear. Therefore, the purpose of this project is to investigate the behavioral response of rats with an overexpression of △FosB in the nucleus accumbens (NAc) shell in sucrose and cocaine self-administration.
Methods: Twenty Sprague Dawley rats were injected with eitherAAV overexpressing △FosB or control AAV in the NAc shell. Rats were allowed to respond for sucrose pellets under FR1 and PR schedules both in a hunger motivated state (85% free feed body weight) and a non-hunger motivated state (free feed weight). Then animals self administered cocaine in sessions of acquisition, extinction, and dose response under FR1, FR5 and PR schedules.
Results: Our results demonstrate that rats with △FosB overexpression in the NAc shell responded more for sucrose pellets than control rats on an FR1 schedule when they were in a hunger motivated state. However, △FosB rats responded less for sucrose pellets in progressive ratio when they were at their free feed weight, which is similar to the sucrose responding of enriched rats. In cocaine self-administration, rats with △FosB overexpression in the NAc shell exhibit less drug-seeking behavior. Ongoing experiments are testing cocaine cue reactivity following abstinence.
Conclusions: Overexpressing ΔFosB in the NAc shell decreases cocaine-taking behavior and mimics the protective addiction phenotype of environmental enrichment.
Financial Support: This grant is funded by NIDA and supported by DA029091.

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STRUCTURE-ACTIVITY RELATIONSHIP STUDIES ON THE TETRAHYDROISOQUINOLINE-BASED OREXIN 1 RECEPTOR ANTAGONISTS: THE 1-BENZYL POSITION.

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Aims: Blockade of the OX1 receptor has been suggested to be a promising strategy for the treatment of drug addiction. To develop potent and selective OX1 antagonist, we have performed structure-activity relationship studies on the tetrahydroisoquinoline scaffold, the core structure in both the dual OX1/OX2 receptor antagonist ACT-078573 and the OX2 selective antagonist TCS-OX2-29. Recently we described the synthesis and in vitro and in vivo characterization of a series of analogs some of which showed excellent potency at and selectivity for the OX1 receptor. We herein report our efforts in further exploring the structural requirements for receptor subtype selectivity focusing on the 1-benzyl position of the tetrahydroisoquinoline.
Methods: All target compounds were synthesized and characterized by MS, NMR and HPLC. Target compounds were evaluated in calcium-dependent functional assays in RD-HGA16 (Molecular Devices) cell lines stably expressing either the OX1 or OX2 receptor.
Results: Structural features important for OX1 potency and selectivity have been identified including the requirement for aromatic functionality at this 1-position. Among synthesized compounds, several showed low nanomolar potency at the OX1 receptor and good selectivity over the OX2 receptor.
Conclusions: Further SAR studies on the tetrahydroisoquinolines have resulted in several compounds that are potent and OX1 selective. Structural features that determine OX1 potency and selectivity at the 1-position have been identified. These finding will expedite the development of potent and selective OX1 antagonists as medications for the treatment of OX1-mediated disorders such as drug addiction.
Financial Support: NIH grants DA032837 and DA026582.

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ALCOHOL DRINKING AND RELATED BEHAVIORS IN HYPOTHALAMIC-SPECIFIC POMC-DEFICIENT MICE.

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Aims: Opioidergic mechanisms, particularly involving beta-endorphin (B-EP) and mu opioid receptor, are critically involved in motivational behaviors. The opioid receptor antagonist naltrexone reduces alcohol consumption and relapse both in humans and in rodent models of excessive alcohol intake. Alcohol-preferring mice show higher proopiomelanocortin (Pomc) gene expression in arcuate nucleus of hypothalamus than their non-preferring counterparts. We hypothesize that alcohol-induced changes of hypothalamic POMC neurons (possibly also other areas) play a critical role in alcohol drinking behaviors.
Methods: Using C57BL/6J mice with targeted deletion of the Pomc neuronal enhancers nPE1 and nPE2 (nPE-/-), resulting in hypothalamic-specific Pomc and central B-EP deficiency, but intact pituitary Pomc expression, we determined alcohol consumption/preference, sucrose and saccharin consumptions, with a drinking-in-the-dark (DID) protocol. DID and alcohol-induced conditioned place preference (CPP) were tested in nPE+/+ mice with naltrexone (0.4-10 mg/kg) or kappa receptor antagonist nor-BNI (1-5 mg/kg).
Results: nPE+/+ mice exposed to alcohol at 7.5%, 15% and 30% concentrations showed high alcohol preference (preference ratios 0.6-0.7) and rapidly established stable alcohol drinking behavior: males and females consumed daily 4-6 g/kg/4-h and 8-10 g/kg/4-h pure alcohol, respectively. In contrast, both sexes of nPE-/- had significantly less alcohol preference (ratios<0.2-0.3), less consumption (<2-3 g/kg/4-h) and correspondingly lower blood ethanol levels. nPE-/- also showed slightly less saccharin drinking, compared with their nPE+/+ littermates. However, both genotypes showed similar sucrose drinking. Consistent with this genetic approach, pharmacological blockade of opioid receptors with naltrexone, but not nor-BNI, dose-dependently reduced alcohol drinking and CPP expression in nPE+/+ mice.
Conclusions: The results suggest that neuronal POMC is essential in alcohol drinking, probably via hypothalamic B-EP-mediated mechanism.
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HIV-1 TRANSGENIC RATS EXHIBIT ATTENUATED COCAINE-MEDIATED INCREASE IN SYNAPTOSOMAL [3H] DOPAMINE UPTAKE IN STRIATUM FOLLOWING COCAINE SELF-ADMINISTRATION.

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Aims: This study explored the potential mechanism(s) underlying the alterations in the dopamine (DA) transporter (DAT) function of HIV-1 transgenic (Tg) rats in response to cocaine.
Methods: In Experiment-1, drug naive male Tg rats and age-matched Fischer 344 (F344) rats were used to determine basal Vmax of [3H]DA uptake, Bmax of [3H]WIN35,428 binding, and cell surface DAT expression in the striatum. In Experiment-2, ovariectimized female Tg and F344 rats underwent cocaine (0.33 mg/kg/infusion, FR-1) or sucrose (5% w/v) self-administration (SA) for 31 days. Synaptosomal [3H]DA uptake in rat prefrontal cortex (PFC) and striatum was examined 24 hr after the final SA session.
Results: In Experiment-1 the Vmax was increased (51%) in striatum of Tg rats compared to F344 rats. Total DATs were not different between Tg and F344 rats but the cell surface DAT was increased (24%) in striatum of Tg rats. Tg rats showed decreased Bmax (24%) along with the increased Vmax, which suggests an increase in DA uptake turnover rate (Vmax/Bmax). Prior sucrose SA experience increased (41%) Vmax in striatum, but not in PFC, of Tg rats relative to F344 rats. Compared to sucrose, F344 rats self-administering cocaine exhibited increased Vmax (60%) in striatum but not in PFC, whereas Vmax were not altered in striatum, but decreased by 70% in PFC, of cocaine self-administering Tg rats.
Conclusions: Tg rats exhibit neuroadaptive changes in striatal DAT function under basal conditions with an increased DA uptake turnover rate and cell surface DAT expression, perhaps compensating for their damaged DAT function by HIV-1 viral proteins. However, Tg rats did not show increased DA uptake in response to cocaine-mediated elevations in DA as seen in F344 rats. Thus, Tg rats represent a unique model for studying the effects of HIV-1 viral proteins on in vivo DAT function and cocaine-mediated behavior.
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EFFECTS OF THE COMBINATION OF EXERCISE (WHEEL RUNNING) AND ATOMOXETINE ON COCAINE-SEEKING BEHAVIOR IN RATS.

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Aims: Evidence suggests that the combination of behavioral and pharmacological therapies for addiction might be more efficacious than individual therapies alone. Aerobic exercise and the atomoxetine are two monotherapies that have been shown to suppress reinstatement of cocaine seeking in an animal model of relapse. The purpose of the present study was to determine whether the combination of exercise and atomoxetine would be more effective than either treatment alone in animals with differing susceptibility to drug abuse (i.e., high vs. low impulsive rats). The present study investigated the effects of combining exercise and atomoxetine on cocaine-seeking behavior precipitated by cocaine and cocaine-paired cues in rats selected for high or low impulsivity on a delay discounting task.
Methods: Rats were screened for high impulsivity (HiI, N = 14) or low impulsivity (LoI, N = 9) on a delay discounting task for food reward, and then they were implanted with chronic indwelling jugular catheters and trained to self-administer cocaine (0.4 mg/kg/infusion) under a fixed-ratio 1 schedule during 6-h daily sessions for 10 days. Subsequently, cocaine access was removed, and cocaine-paired cues (e.g., house light, stimulus lights, infusion pump) were discontinued for 14 days to allow rats to extinguish responding. Next, both groups were tested in a within-subjects design for reinstatement of cocaine-seeking precipitated by separate administration of cocaine or cocaine-paired cues in the presence of concurrent running wheel access (W), pretreatment with atomoxetine (A), or both (W+A).
Results: LoI rats showed greater cue-induced reinstatement compared to HiI rats, but there were no phenotype differences in cocaine-primed reinstatement. Both individual treatments and the combination treatment, W+A, significantly attenuated cue-induced cocaine seeking. However, only W+A was effective in reducing cocaine-induced cocaine seeking.
Conclusions: Combined behavioral (exercise) and pharmacological (atomoxetine) treatments are more effective than each individual treatment alone.
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CIGARETTE SMOKING AND THE ONSET AND PERSISTENCE OF MAJOR DEPRESSIVE DISORDER AMONG ADULTS IN THE UNITED STATES: 1994-2005.

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Aims: The present study sought to investigate whether cigarette smoking is (a) associated with increased risk of onset and persistence of major depressive disorder (MDD) and whether smoking cessation maintenance reduces the risk of onset and persistence of MDD over a 10 year period among adults in the United States.
Methods: Data were drawn from the Midlife Development in the United States Survey (MIDUS) Waves I and II (N=2, 101). Logistic regression analyses were used to investigate the relations between smoking and the onset and persistent of MDD, adjusting for demographic characteristics and substance use problems.
Results: Daily smoking in 1994 and persistent daily smoking (from 1994 to 2005) predicted a significantly increased likelihood of past-year incident and persistent MDD by 2005. These associations largely remained statistically significant after adjusting for demographics and substance use problems. Sucessful smoking abstention significantly reduced the risk of recent incidence and persistence of MDD.
Conclusions: The present logitudinal data provide novel insights into the role of smoking in the onset and persistence of MDD. Namely, smoking is associated with a significant increased risk of MDD and quitting helps to reduce such risk. Specifically, the longer the duration of abstinence/ successful quitting, the lower the risk of subsequent onset of MDD. The mental health benefits of quitting smoking in the form of reduced risk of MDD should be added to common information listed as the reasons to quit.
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